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=> fil capl; d que l3; d que l12; d que l14; s l3 or l12 or l14; fil wpids; d que l46; d
que l53; s l46 or l53
FILE 'CAPLUS' ENTERED AT 16:53:17 ON 24 APR 2002
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FILE COVERS 1907 - 24 Apr 2002  VOL 136 ISS 17
FILE LAST UPDATED: 23 Apr 2002  (20020423/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
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the CAS Roles thesaurus (/RL field) in this file.

L1          827 SEA FILE=CAPLUS ABB=ON  OWEN D?/AU
L2           41 SEA FILE=CAPLUS ABB=ON  BYRNE N?/AU
L3            2 SEA FILE=CAPLUS ABB=ON  L1 AND L2


L1          827 SEA FILE=CAPLUS ABB=ON  OWEN D?/AU
L2           41 SEA FILE=CAPLUS ABB=ON  BYRNE N?/AU
L4         5043 SEA FILE=CAPLUS ABB=ON  ANALYTICAL APPARATUS+OLD/CT
L5        84006 SEA FILE=CAPLUS ABB=ON  ELECTRIC RESISTANCE/CT OR ELECTRIC
              IMPEDANCE/CT
L6        70158 SEA FILE=CAPLUS ABB=ON  ELECTRODES/CT
L7        25641 SEA FILE=CAPLUS ABB=ON  MEMBRANE, BIOLOGICAL/CT
L8        21694 SEA FILE=CAPLUS ABB=ON  ION CHANNEL+OLD/CT
L9         2185 SEA FILE=CAPLUS ABB=ON  ANION CHANNEL/CT OR CHLORIDE CHANNEL/CT

L10       17473 SEA FILE=CAPLUS ABB=ON  CATION CHANNEL/CT OR CALCIUM CHANNEL/CT
               OR POTASSIUM CHANNEL/CT OR SODIUM CHANNEL/CT
L11       38195 SEA FILE=CAPLUS ABB=ON  TRANSPORT?(L)(ION? OR ANION? OR
              CATION?)/OBI
L12           1 SEA FILE=CAPLUS ABB=ON  (L1 OR L2) AND L7 AND ((L4 OR L5 OR
              L6) OR (L8 OR L9 OR L10 OR L11))


L1          827 SEA FILE=CAPLUS ABB=ON  OWEN D?/AU
L2           41 SEA FILE=CAPLUS ABB=ON  BYRNE N?/AU
L7        25641 SEA FILE=CAPLUS ABB=ON  MEMBRANE, BIOLOGICAL/CT
L13          25 SEA FILE=CAPLUS ABB=ON  9/SC,SX AND (L1 OR L2)
L14           2 SEA FILE=CAPLUS ABB=ON  L13 AND L7
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Section code - Biochemical methods

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L205          3 L3 OR L12 OR L14


FILE 'WPIDS' ENTERED AT 16:53:18 ON 24 APR 2002
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FILE LAST UPDATED: 18 APR 2002              <20020418/UP>
MOST RECENT DERWENT UPDATE          200225   <200225/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

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L44           170 SEA FILE=WPIDS ABB=ON  OWEN D?/AU
L45            28 SEA FILE=WPIDS ABB=ON  BYRNE N?/AU
L46             2 SEA FILE=WPIDS ABB=ON  L45 AND L44



L44           170 SEA FILE=WPIDS ABB=ON  OWEN D?/AU
L45            28 SEA FILE=WPIDS ABB=ON  BYRNE N?/AU
L47        109869 SEA FILE=WPIDS ABB=ON  MEMBRANE#
L51          2153 SEA FILE=WPIDS ABB=ON  (ION## OR CATION## OR ANION##)(2A)(CHANN
                 EL# OR TRANSPORT?)
L52          1935 SEA FILE=WPIDS ABB=ON  (CALCIUM OR CHLORIDE OR POTASSIUM OR
                 SODIUM)(2A)(CHANNEL# OR TRANSPORT?)
L53             2 SEA FILE=WPIDS ABB=ON  (L44 OR L45) AND L47 AND (L51 OR L52)


L206          2 L46 OR L53

=> fil medl; d que l70; d que l73; d que l75; fil biosis; d que l106; d que l107;s l106
or l107
FILE 'MEDLINE' ENTERED AT 16:53:46 ON 24 APR 2002

 FILE LAST UPDATED: 23 APR 2002 (20020423/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
```

Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

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L68          525 SEA FILE=MEDLINE ABB=ON  OWEN D?/AU
L69           41 SEA FILE=MEDLINE ABB=ON  BYRNE N?/AU
L70            0 SEA FILE=MEDLINE ABB=ON  L68 AND L69


L64        36680 SEA FILE=MEDLINE ABB=ON  ELECTRODES+NT/CT
L65         3245 SEA FILE=MEDLINE ABB=ON  ELECTRIC IMPEDANCE/CT
L66        61198 SEA FILE=MEDLINE ABB=ON  ION CHANNELS+NT/CT
L67         6989 SEA FILE=MEDLINE ABB=ON  ION TRANSPORT+NT/CT
L68          525 SEA FILE=MEDLINE ABB=ON  OWEN D?/AU
L69           41 SEA FILE=MEDLINE ABB=ON  BYRNE N?/AU
L71       170127 SEA FILE=MEDLINE ABB=ON  MEMBRANES+NT/CT
L73            0 SEA FILE=MEDLINE ABB=ON  (L68 OR L69) AND ((L64 OR L65 OR L66
                  OR L67)) AND L71


L64        36680 SEA FILE=MEDLINE ABB=ON  ELECTRODES+NT/CT
L65         3245 SEA FILE=MEDLINE ABB=ON  ELECTRIC IMPEDANCE/CT
L66        61198 SEA FILE=MEDLINE ABB=ON  ION CHANNELS+NT/CT
L67         6989 SEA FILE=MEDLINE ABB=ON  ION TRANSPORT+NT/CT
L68          525 SEA FILE=MEDLINE ABB=ON  OWEN D?/AU
L69           41 SEA FILE=MEDLINE ABB=ON  BYRNE N?/AU
L75            1 SEA FILE=MEDLINE ABB=ON  (L68 OR L69) AND (L64 OR L65) AND
                  ((L66 OR L67))


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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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RECORDS LAST ADDED: 17 April 2002 (20020417/ED)


L104         706 SEA FILE=BIOSIS ABB=ON  OWEN D?/AU
L105          57 SEA FILE=BIOSIS ABB=ON  BYRNE N?/AU
L106           2 SEA FILE=BIOSIS ABB=ON  L104 AND L105


L100        4078 SEA FILE=BIOSIS ABB=ON  ELECTRIC?(2A)(RESIST? OR IMPED?)
L101       52749 SEA FILE=BIOSIS ABB=ON  ELECTRODE?
L102      126369 SEA FILE=BIOSIS ABB=ON  (ION? OR CATION? OR ANION? OR CALCIUM
                  OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR TRANSPORT?)

L103      775872 SEA FILE=BIOSIS ABB=ON  MEMBRANE#
L104         706 SEA FILE=BIOSIS ABB=ON  OWEN D?/AU
L105          57 SEA FILE=BIOSIS ABB=ON  BYRNE N?/AU
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L107          2 SEA FILE=BIOSIS ABB=ON  (L104 OR L105) AND L103 AND L102 AND
                (L100 OR L101)


L207          3 L106 OR L107

=> fil biotechno; d que l131; d que l181; d que l180
FILE 'BIOTECHNO' ENTERED AT 16:54:03 ON 24 APR 2002
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FILE LAST UPDATED: 16 APR 2002      <20020416/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<


L129         64 SEA FILE=BIOTECHNO ABB=ON  OWEN D?/AU
L130          5 SEA FILE=BIOTECHNO ABB=ON  BYRNE N?/AU
L131          0 SEA FILE=BIOTECHNO ABB=ON  L129 AND L130



L125        346 SEA FILE=BIOTECHNO ABB=ON  ELECTRIC?(2A)(IMPED? OR RESIST?)
L126       4501 SEA FILE=BIOTECHNO ABB=ON  ELECTRODE#
L127     143990 SEA FILE=BIOTECHNO ABB=ON  MEMBRANE#
L128      25485 SEA FILE=BIOTECHNO ABB=ON  (ION? OR CATION? OR ANION? OR
                CALCIUM OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR
                TRANSPORT?)
L130          5 SEA FILE=BIOTECHNO ABB=ON  BYRNE N?/AU
L181          0 SEA FILE=BIOTECHNO ABB=ON  L130 AND (L125 OR L126 OR L127 OR
                L128)



L125        346 SEA FILE=BIOTECHNO ABB=ON  ELECTRIC?(2A)(IMPED? OR RESIST?)
L126       4501 SEA FILE=BIOTECHNO ABB=ON  ELECTRODE#
L127     143990 SEA FILE=BIOTECHNO ABB=ON  MEMBRANE#
L128      25485 SEA FILE=BIOTECHNO ABB=ON  (ION? OR CATION? OR ANION? OR
                CALCIUM OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR
                TRANSPORT?)
L133         11 SEA FILE=BIOTECHNO ABB=ON  "OWEN D G"/AU
L180          3 SEA FILE=BIOTECHNO ABB=ON  L127 AND L133 AND (L125 OR L126 OR
                L128)


=> fil embase; d que l138; d que l160
=> fil embase
FILE 'EMBASE' ENTERED AT 16:57:09 ON 24 APR 2002
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 FILE COVERS 1974 TO 18 Apr 2002 (20020418/ED)

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 substance identification.

=> d que l138; d que l160
L136        410 SEA FILE=EMBASE ABB=ON  OWEN D?/AU
L137         46 SEA FILE=EMBASE ABB=ON  BYRNE N?/AU
L138          0 SEA FILE=EMBASE ABB=ON  L136 AND L137
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L136          410 SEA FILE=EMBASE ABB=ON  OWEN D?/AU
L137           46 SEA FILE=EMBASE ABB=ON  BYRNE N?/AU
L157          775 SEA FILE=BIOSIS ABB=ON  (TRANS EPITHELIAL OR TRANSEPITHELIAL)(W
                  )RESISTANCE
L160            0 SEA FILE=EMBASE ABB=ON  L157 AND (L136 OR L137)


=> dup rem l75,l205,l180,l207,l206
FILE 'MEDLINE' ENTERED AT 16:58:50 ON 24 APR 2002

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PROCESSING COMPLETED FOR L205
COMMAND INTERRUPTED

=> dup rem l75,l205,l180,l207,l206
PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L205
PROCESSING COMPLETED FOR L180
PROCESSING COMPLETED FOR L207
PROCESSING COMPLETED FOR L206
L208            9 DUP REM L75 L205 L180 L207 L206 (3 DUPLICATES REMOVED)
                  ANSWER '1' FROM FILE MEDLINE
                  ANSWERS '2-4' FROM FILE CAPLUS
                  ANSWERS '5-7' FROM FILE BIOTECHNO
                  ANSWERS '8-9' FROM FILE BIOSIS

=> d ibib ab l208 1-9

L208 ANSWER 1 OF 9     MEDLINE
ACCESSION NUMBER:    93364671     MEDLINE
DOCUMENT NUMBER:     93364671   PubMed ID: 8358568
TITLE:               Pharmacology of a cloned potassium channel from mouse brain
                     (MK-1) expressed in CHO cells: effects of blockers and an
                     'inactivation peptide'.
AUTHOR:              Robertson B; Owen D G
CORPORATE SOURCE:    Electrophysiology Laboratory, Wyeth Research, Taplow,
                     Maidenhead.
SOURCE:              BRITISH JOURNAL OF PHARMACOLOGY, (1993 Jul) 109 (3) 725-35.
                     Journal code: B00; 7502536. ISSN: 0007-1188.
PUB. COUNTRY:        ENGLAND: United Kingdom
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199309
ENTRY DATE:          Entered STN: 19931015
                     Last Updated on STN: 19931015
                     Entered Medline: 19930928
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AB 1. Chinese hamster ovary cells (CHO), maintained in cell culture, were stably transfected with DNA for the MK-1 voltage-activated potassium channel, previously cloned from a mouse brain library. 2. Voltage-activated currents were recorded by the whole cell patch clamp method. In CHO cells transfected with the vector only, there were no significant outward voltage activated currents. However, large outward voltage-activated potassium currents were always observed in those cells which had been transfected with the vector containing the DNA encoding for MK-1. 3. These potassium currents activated from -40 mV, and reversed at the potassium equilibrium potential. The half-maximal conductance of MK-1 was at -10 mV and had a slope factor of 11 mV when fitted with a Boltzmann function. There was only very slight (< 10%) inactivation of MK-1 even at very large positive voltages. 4. MK-1 was reversibly blocked by: 4-aminopyridine (4-AP, 0.1-4 mM), Toxin I 10-100 nM), mast cell degranulating peptide (1 microM), tetraethylammonium (TEA, 4-10 mM), tedisamil (100 microM), quinine (100 microM) and ciclazindol (100 microM); all applied to the outside of the cell from a 'U tube' rapid perfusion system. 4-AP may block closed as well as open MK-1 potassium channels. 5. A synthetic 20 amino acid peptide derived from the N-terminus sequence of the Shaker B potassium channel (the 'inactivation peptide') produced dramatic inactivation of MK-1 when applied to the inside, but not the outside of the cell. Reducing peptide concentration or 'degrading' the peptide produced less inactivation. 6. The block of MK-1 by the synthetic inactivation peptide was quite different in time dependence from block by internal TEA (0.4-4 mM), which probably blocks much more quickly but less potently than the peptide.

L208 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:396510 CAPLUS
TITLE: Interface patch clamping
INVENTOR(S): **Byrne, Nicholas Gerard; Owen, David Geraint**
PATENT ASSIGNEE(S): Cenes Limited, UK
SOURCE: PCT Int. Appl.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034776	A1	20000615	WO 1999-GB4073	19991206
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141704	A1	20011010	EP 1999-958379	19991206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
NO 2001002766	A	20010806	NO 2001-2766	20010605

PRIORITY APPLN. INFO.:
GB 1998-26742 A 19981205
GB 1999-5998 A 19990317
GB 1999-6053 A 19990317
WO 1999-GB4073 W 19991206

AB The invention provides a novel development of the conventional patch clamp technique for measurement of whole cell electrical activity. The invention provides for one or more cell or cells to be suspended in a

liquid medium at a liquid/air interface (by virtue of the effect of surface tension at the interface) whereby the cell or cells are accessible at the interface to a microstructure electrode (such as a pipette tip) to which a cell can attach to form an electrical seal, for the purpose of whole cell voltage clamp recording. According to the invention the electrode can be caused to form a high resistance electrical seal with a cell suspended in the liquid at the liquid/air interface without the need to press the cell against a solid support surface. The invention also provides apparatus for carrying out the interface patch clamp technique and control logic for operating a computer to carry out the interface patch clamp technique.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L208 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1999:811453 CAPLUS
DOCUMENT NUMBER: 132:32906
TITLE: High throughput screen for membrane ion channels
INVENTOR(S): **Owen, David Geraint; Byrne, Nicholas Gerard**
PATENT ASSIGNEE(S): Cenes Limited, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9966329	A1	19991223	WO 1999-GB1871	19990614
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9942835	A1	20000105	AU 1999-42835	19990614
EP 1084410	A1	20010321	EP 1999-957097	19990614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
NO 2000006295	A	20010212	NO 2000-6295	20001211

PRIORITY APPLN. INFO.: GB 1998-12783 A 19980612
WO 1999-GB1871 W 19990614

AB The present invention relates to a structure comprising a biol. membrane and a porous or perforated substrate, a biol. membrane, a substrate, a high throughput screen, methods for prodn. of the structure membrane and substrate, and a method for screening a large no. of test compds. in a short period. More particularly it relates to a structure comprising a biol. membrane adhered to a porous or perforated substrate, a biol. membrane capable of adhering with high resistance seals to a substrate such as perforated glass and the ability to form sheets having predominantly an ion channel or transporter of interest, a high throughput screen for detg. the effect of test compds. on ion channel or transporter activity, methods for manuf. of the structure, membrane and substrate, and a method for monitoring ion channel or transporter activity in a membrane.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L208 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:67277 CAPLUS
DOCUMENT NUMBER: 132:248183
TITLE: Bioorganic synthesis of lipid-modified proteins for the study of signal transduction
AUTHOR(S): Bader, Benjamin; Kuhn, Karsten; **Owen, David J.**; Waldmann, Herbert; Wittinghofer, Alfred; Kuhlmann, Jurgen
CORPORATE SOURCE: Max-Planck Institut fur Molekulare Physiologie, Dortmund, 44227, Germany
SOURCE: Nature (London) (2000), 403(6766), 223-226
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biol. membranes define the boundaries of the cellular compartments in higher eukaryotes and are active in many processes such as signal transduction and vesicular transport. Although post-translational lipid modification of numerous proteins in signal transduction is crucial for biol. function, anal. of protein-protein interactions has mainly focused on recombinant proteins in soln. under defined in vitro conditions. Here we present a new strategy for the synthesis of such lipid-modified proteins. It involves the bacterial expression of a carboxy-terminally truncated non-lipidated protein, the chem. synthesis of differently lipidated peptides representing the C terminus of the proteins, and their covalent coupling. Our technique is demonstrated using Ras constructs, which exhibit properties very similar to fully processed Ras, but can be produced in high yields and are open for selective modifications. These constructs are operative in biophys. and cellular assay systems, showing specific recognition of effectors by Ras lipoproteins inserted into the membrane surface of biosensors and transforming activity of oncogenic variants after microinjection into cultured cells.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L208 ANSWER 5 OF 9 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1994:24186571 BIOTECHNO
TITLE: On the mechanism of 4-aminopyridine action on the cloned mouse brain **potassium channel** mKv1.1
AUTHOR: Stephens G.J.; Garratt J.C.; Robertson B.; **Owen D.G.**
CORPORATE SOURCE: Electrophysioloyy Laboratory, Wyeth Research (UK), Huntercombe Lane South,Taplow, Berkshire SL6 0PH, United Kingdom.
SOURCE: Journal of Physiology, (1994), 477/2 (187-196)
CODEN: JPHYA7 ISSN: 0022-3751
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AB 1. This study used the whole-cell patch clamp technique to investigate the mechanism of action of the K.sup.+ channel blocker 4-aminopyridine (4-AP) on the cloned K.sup.+ channel mouse Kv1.1 (mKv1.1) expressed in Chinese hamster ovary cells. 2. Cells transfected with mKv1.1 expressed a non-inactivating, delayed rectifier-type K.sup.+ current. 4-AP induced a dose-, voltage- and use-dependent block of mKv1.1. 3. 4-AP blockade of mKv1.1 was similar whether 4-AP was administered extracellularly (IC.sub.5.sub.0 = 147 .mu.M) or intracellularly (IC.sub.5.sub.0 = 117 .mu.M). 4. Inclusion of the first twenty amino acids of the N-terminus sequence of the Shaker B K.sup.+ channel ('inactivation peptide') in the patch **electrode** transformed mKv1.1 into a rapidly inactivating current. The time constant of decay for the modified current was dependent on the concentration of inactivation peptide, and under these

conditions extracellular 4-AP had a reduced potency (IC.sub.5.sub.0 values of 471 and 537 .mu.M for 0.5 and 2 mg ml.sup.-.sup.1 inactivation peptide, respectively). 5. A permanently charged analogue of 4-AP, 4-aminopyridine methiodide (4-APMI), was found to block mKv1.1 when applied inside the cell, but was without effect when administered externally. 6. Decreasing the intracellular pH (pH(i)) to 6.4 caused an increase in 4-AP potency (IC.sub.5.sub.0 = 76 .mu.M), whereas at PH(i) 9.0, the 4-AP potency fell (IC.sub.5.sub.0 = 295 .mu.M). Conversely, increasing extracellular pH (pH(o)) to 9.0 caused an increase in 4-AP potency (IC.sub.5.sub.0 = 93 .mu.M), whereas at pH(o) 6.4, 4-AP potency decreased (IC.sub.5.sub.0 = 398 .mu.M). 7. Taken together, these findings support the hypotheses that the uncharged form of 4-AP crosses the **membrane**, and that it is predominantly the cationic form which acts on mKv1.1 channels intracellularly, possibly at or near to the binding site for the inactivation peptide.

L208 ANSWER 6 OF 9 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1996:26345583 BIOTECHNO
TITLE: Studies on the blocking action of human Kv3.4 inactivation peptide variants in the mouse cloned Kv1.1 K.sup.+ channel
AUTHOR: Stephens G.J.; **Owen D.G.**; Opalko A.; Pisano M.R.; MacGregor W.H.; Robertson B.
CORPORATE SOURCE: Department of Pharmacology, Royal Free Hospital, School of Medicine, Rowland Hill Street,London NW3 2PF, United Kingdom.
SOURCE: Journal of Physiology, (1996), 496/1 (145-154)
CODEN: JPHYA7 ISSN: 0022-3751
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AB 1. Whole-cell patch clamp recordings were made from Chinese hamster ovary (CHO) cells stably expressing homomeric mouse Kv1.1 (delayed rectifier K.sup.+; mKv1.1) channels. The effects of internal application of a number of different peptides, based on part of the amino terminal sequence of the human Kv3.4 channel subunit (hKv3.4), were examined in order to determine their influence on N-type inactivation. 2. For the native hKv3.4 peptide, the association rate constant (k(on)) increased with **membrane** depolarization, whilst the dissociation rate constant (k(off)) had little dependence on voltage. This resulted in the apparent dissociation constant (K(D)) of the hKv3.4 peptide tending to increase with depolarization. 3. In general, k(on) increased and apparent K(D) decreased with positive charge of the hKv3.4 peptide variants; in peptides lacking a hydrophobic amino terminal this correlation was not maintained. In contrast, the rate of dissociation of the variant peptides (k(off)) was independent of net charge. 4. The blocking activity of the hKv3.4 peptide was not dependent on a disulphide bridge between cysteine residues C6 and C24 and the presence of cysteine residues in the hKv3.4 peptide was not a prerequisite for rapid inactivation. All cysteine-substituted variants, especially at C6, showed a more rapid recovery from inactivation than the hKv3.4 peptide. Substitutions at C24, and not C6, reduced k(on). 5. The present results concerning the action of the mammalian hKv3.4 channel inactivation particle on mKv1.1 channels complement earlier models for the invertebrate Shaker K.sup.+ channel. It is proposed that the hydrophobic amino terminal region of the hKv3.4 inactivation peptide blocks the channel pore, whilst the adjacent positively charged region interacts with negative charges on the channel protein.

L208 ANSWER 7 OF 9 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1987:18137013 BIOTECHNO
TITLE: Signals transduced by .gamma.-aminobutyric acid in

cultured central nervous system neurons and thyrotropin releasing hormone in clonal pituitary cells

AUTHOR: Barker J.L.; Dufy B.; Harrington J.W.; Harrison N.L.; MacDermott A.B.; MacDonald J.F.; **Owen D.G.**; Vincini S.

CORPORATE SOURCE: Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892, United States.

SOURCE: Annals of the New York Academy of Sciences, (1987), 494/- (1-38)
CODEN: ANYAA0 ISSN: 0077-8923

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have briefly reviewed recent studies into two quite different signal transduction mechanisms recorded in nerve and endocrine cells. One is seemingly ubiquitous, being observed at many synapses in circuits and systems throughout the vertebrate CNS. Most of this amino-acid-mediated signal appears to be transduced at the subsynaptic plasma **membrane** where receptors rapidly couple micromolar GABA to proteins gating Cl.sup.- **ion channel** mechanisms and so trigger inhibitory pauses in ambient electrical activity each lasting several to tens of milliseconds. Such signals would serve to suppress action-potential-evoked output from CNS neurons. These synaptic signals are modulated by clinically important drugs and naturally occurring steroids through effects on Cl.sup.- **ion channel** gating kinetics. The other is a hormonal signal transduced in a prolactin/growth hormone-secreting clone of pituitary origin by nanomolar TRH. This peptide-mediated signal is ipso facto extrasynaptic, noticeably delayed in onset when detected electrically and lasts several minutes, not milliseconds. TRH receptor engagement initially activates K.sup.+ channels and inactivates voltage-gated Ca.sup.2.sup.+ channels for tens of seconds. These effects are most likely derived from hydrolysis of phosphoinositide substrate in the plasma **membrane** and subsequent generation of an intracellular messenger (1,4,5-IP3) that mobilizes Ca.sup.2.sup.+ from cytoplasmic stores, the free Ca then diffusing to the plasma **membrane** to modulate K.sup.+ and Ca.sup.2.sup.+ channel activities. A second phase of electrical activity consisting of low-amplitude voltage fluctuations and action potential activity at the level of the resting potential can be mimicked by ligands that activate PKC. Presumably, TRH receptor mediated hydrolysis of phosphatidyl inositol-4,5-bisphosphate generating DAG provides a naturally occurring second messenger to activate PKC, which in turn may phosphorylate **membrane** proteins and thereby enhance electrical excitability. All of these **membrane** actions are temporally associated with a several-fold increase in prolactin output lasting minutes. The fast synaptic and slow extrasynaptic chemically mediated signals outlined here may well be representative of two important classes of intercellular communication critical to many functions expressed by the vertebrate CNS.

L208 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:493051 BIOSIS

DOCUMENT NUMBER: PREV200100493051

TITLE: Automated **ion channel** screening by Interface-Patch(TM) clamping.

AUTHOR(S): **Owen, D. (1)**; Mitchell, R. (1); Piotrowski, V. (1); Norwood, J. (1); Collie, I. (1); Plant, K. (1); Tomlin, A. (1); Daum, P. (1); Nichols, J. (1); Elsegood, K. (1); Bennett, R. (1); Silverthorne, A. (1); **Byrne, N.**

(1)
CORPORATE SOURCE: (1) CeNeS Ltd, Cambridge UK
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 712. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Ion channels** are increasingly important targets in drug discovery. Although the definitive way of measuring **ion channel** activity, electrophysiological techniques such as patch-clamping are slow and labour intensive and therefore impractical for drug discovery programmes. Fluorescence techniques have speeded up throughput of some **ion channel** assays but false hits and misses are a problem, in part reflecting the relatively poor time and amplitude resolution compared with patch-clamp, and the inherent lack of voltage control. In any case a bottleneck remains downstream when hits have to be evaluated in electrophysiological systems. We have developed an automated patch-clamp system (AutoPatch) that uses the novel Interface-Patch process in which the recording **electrode** is inverted and contacts a suspension of cells. The system controls all aspects of patch-clamping from seal formation through to drug application including on-line analysis to facilitate rapid data analysis. AutoPatch has de-skilled patch-clamping with concomitant reduction in human resource costs and improved quality control. The current workstation (AP1) can be bench mounted as it is compact (footprint 30cm) and vibration-insensitive. The system has already been applied to a variety of cells including CHOs and HEK-293s and assays for **ion channels** such as Nav1.3, Kv1.1 and hERG have been validated. A miniaturised multi-well design (AP2) will also be described. The AP2 disposable plate system will form the basis of a massively parallel AutoPatch (AP3) which promises 1000X the throughput of conventional patch-clamping.

L208 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:497830 BIOSIS
DOCUMENT NUMBER: PREV200100497830
TITLE: Automated hERG ion channel screening using the AutoPatch(TM.
AUTHOR(S): Plant, K. (1); Bennett, R. (1); Elsegood, K. (1); **Byrne, N. (1)**; Marchionni, M. (1); **Owen, D.** (1)
CORPORATE SOURCE: (1) CeNeS Ltd, Cambridge UK
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 712. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The hERG voltage-gated potassium channel is one of several K+ channels which orchestrate the shaping of the cardiac action potential. Expression abnormalities of the hERG channel are linked to long QT syndrome (LQTS) and it appears that LQTS can also be drug-induced via block of the hERG channel. Electrophysiological assays are recommended by regulatory bodies to pick up this potential side effect prior to testing in human volunteers. Unfortunately, traditional patch-clamping of cells expressing hERG is slow even for the relatively small numbers of late-stage compounds requiring this type of screen and certainly impractical in early stage

screening of large libraries of compounds. Furthermore, significant variability exists in data obtained between labs providing screening services. To over come these limitations without compromising the quality of data, we have developed an assay to screen hERG using the AutoPatch(TM), an automated patch-clamp which uses Interface Patch(TM) Clamp technology (Owen et al this meeting). hERG channels expressed in HEK-293 cells were grown using standard tissue culture methods and resuspended for use in the AutoPatch. Cells were also patch-clamped using a conventional rig for comparison. The physiological characteristics of hERG were indistinguishable from conventionally-patched cells and IC50's for E-4031 and terfenadine in the AutoPatch system were 138nM and 25nM, respectively, compared with 123nM and 20nM, respectively, with the conventional rig. The successful implimentation of a hERG assay using the AutoPatch, enables automated hERG screening with associated quality assurance now, and the transfer to a high-throughput AutoPatch platform in the near future.

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FILE COVERS 1907 - 24 Apr 2002  VOL 136 ISS 17
FILE LAST UPDATED: 23 Apr 2002  (20020423/ED)

  This file contains CAS Registry Numbers for easy and accurate
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CAS roles have been modified effective December 16, 2001. Please
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Scientific Instrumentation

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 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
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 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
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FILE COVERS 1969 TO DATE.
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L101      52749 SEA FILE=BIOSIS ABB=ON  ELECTRODE?
L102     126369 SEA FILE=BIOSIS ABB=ON  (ION? OR CATION? OR ANION? OR CALCIUM
                OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR TRANSPORT?)

L103     775872 SEA FILE=BIOSIS ABB=ON  MEMBRANE#
L116      12225 SEA FILE=BIOSIS ABB=ON  L103(8A)L102
L117          1 SEA FILE=BIOSIS ABB=ON  L100 AND L101 AND L116



L100       4078 SEA FILE=BIOSIS ABB=ON  ELECTRIC?(2A)(RESIST? OR IMPED?)
L101      52749 SEA FILE=BIOSIS ABB=ON  ELECTRODE?
L155        775 SEA FILE=BIOSIS ABB=ON  (TRANS EPITHELIAL OR TRANSEPITHELIAL)(W
                )RESISTANCE
L156          4 SEA FILE=BIOSIS ABB=ON  L101 AND L100 AND L155


L212         11 (L108 OR L112 OR L117 OR L156) NOT L207   previously printed

=> fil biotechno; d que l185; d que l203; d que l204; s (l185 or l203) not l180
FILE 'BIOTECHNO' ENTERED AT 17:03:07 ON 24 APR 2002
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FILE LAST UPDATED: 16 APR 2002      <20020416/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<


L125        346 SEA FILE=BIOTECHNO ABB=ON  ELECTRIC?(2A)(IMPED? OR RESIST?)
L126       4501 SEA FILE=BIOTECHNO ABB=ON  ELECTRODE#
L127     143990 SEA FILE=BIOTECHNO ABB=ON  MEMBRANE#
L128      25485 SEA FILE=BIOTECHNO ABB=ON  (ION? OR CATION? OR ANION? OR
                CALCIUM OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR
                TRANSPORT?)
L182       2487 SEA FILE=BIOTECHNO ABB=ON  HIGH(W)(RESIST? OR THROUGH?)
L184        184 SEA FILE=BIOTECHNO ABB=ON  L127 AND (L125 OR L126) AND L128
L185          1 SEA FILE=BIOTECHNO ABB=ON  L184 AND L182



L125        346 SEA FILE=BIOTECHNO ABB=ON  ELECTRIC?(2A)(IMPED? OR RESIST?)
L126       4501 SEA FILE=BIOTECHNO ABB=ON  ELECTRODE#
L128      25485 SEA FILE=BIOTECHNO ABB=ON  (ION? OR CATION? OR ANION? OR
                CALCIUM OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR
                TRANSPORT?)
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L199       2968 SEA FILE=BIOTECHNO ABB=ON  MEMBRANE/CT
L200         47 SEA FILE=BIOTECHNO ABB=ON  MEMBRANES/CW
L203          1 SEA FILE=BIOTECHNO ABB=ON  (L199 OR L200) AND (L125 OR L126)
                AND L128


L125        346 SEA FILE=BIOTECHNO ABB=ON  ELECTRIC?(2A)(IMPED? OR RESIST?)
L126       4501 SEA FILE=BIOTECHNO ABB=ON  ELECTRODE#
L128      25485 SEA FILE=BIOTECHNO ABB=ON  (ION? OR CATION? OR ANION? OR
                CALCIUM OR SODIUM OR CHLORIDE OR POTASSIUM)(2A)(CHANNEL# OR
                TRANSPORT?)
L183         91 SEA FILE=BIOTECHNO ABB=ON  (TRANS EPITHELIAL OR TRANSEPITHELIAL
                )(W)RESISTANCE
L199       2968 SEA FILE=BIOTECHNO ABB=ON  MEMBRANE/CT
L200         47 SEA FILE=BIOTECHNO ABB=ON  MEMBRANES/CW
L202        210 SEA FILE=BIOTECHNO ABB=ON  (L199 OR L200) AND (L125 OR L126 OR
                L128)
L204          0 SEA FILE=BIOTECHNO ABB=ON  L202 AND L183


L213          2 (L185 OR L203) NOT L180   previously printed

=> fil embase; d que l177;d que l175; d que l176;  d que l178; s (l177 or l175 or l176)
FILE 'EMBASE' ENTERED AT 17:03:36 ON 24 APR 2002
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 FILE COVERS 1974 TO 18 Apr 2002 (20020418/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L140      28510 SEA FILE=EMBASE ABB=ON  ION CHANNEL+NT/CT
L163      32883 SEA FILE=EMBASE ABB=ON  CALCIUM TRANSPORT/CT OR SODIUM
                TRANSPORT/CT OR CHLORIDE TRANSPORT/CT OR POTASSIUM TRANSPORT/CT

L164       9187 SEA FILE=EMBASE ABB=ON  ION TRANSPORT/CT
L165     455506 SEA FILE=EMBASE ABB=ON  MEMBRANE#
L166        916 SEA FILE=EMBASE ABB=ON  ELECTRIC RESISTANCE/CT
L167       3850 SEA FILE=EMBASE ABB=ON  IMPEDANCE/CT
L168      16574 SEA FILE=EMBASE ABB=ON  ELECTRODE+NT/CT
L177          5 SEA FILE=EMBASE ABB=ON  (L140 OR L163 OR L164) AND L165 AND
                (L166 OR L167) AND L168


L140      28510 SEA FILE=EMBASE ABB=ON  ION CHANNEL+NT/CT
L159        571 SEA FILE=EMBASE ABB=ON  (TRANS EPITHELIAL OR TRANSEPITHELIAL)(W
                )RESISTANCE
L163      32883 SEA FILE=EMBASE ABB=ON  CALCIUM TRANSPORT/CT OR SODIUM
                TRANSPORT/CT OR CHLORIDE TRANSPORT/CT OR POTASSIUM TRANSPORT/CT

L164       9187 SEA FILE=EMBASE ABB=ON  ION TRANSPORT/CT
L165     455506 SEA FILE=EMBASE ABB=ON  MEMBRANE#
L166        916 SEA FILE=EMBASE ABB=ON  ELECTRIC RESISTANCE/CT
L167       3850 SEA FILE=EMBASE ABB=ON  IMPEDANCE/CT
L168      16574 SEA FILE=EMBASE ABB=ON  ELECTRODE+NT/CT
L174        316 SEA FILE=EMBASE ABB=ON  (L140 OR L163 OR L164) AND L165 AND
                ((L166 OR L167 OR L168))
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L175          2 SEA FILE=EMBASE ABB=ON  L159 AND L174


L140      28510 SEA FILE=EMBASE ABB=ON  ION CHANNEL+NT/CT
L163      32883 SEA FILE=EMBASE ABB=ON  CALCIUM TRANSPORT/CT OR SODIUM
                TRANSPORT/CT OR CHLORIDE TRANSPORT/CT OR POTASSIUM TRANSPORT/CT

L164       9187 SEA FILE=EMBASE ABB=ON  ION TRANSPORT/CT
L165     455506 SEA FILE=EMBASE ABB=ON  MEMBRANE#
L166        916 SEA FILE=EMBASE ABB=ON  ELECTRIC RESISTANCE/CT
L167       3850 SEA FILE=EMBASE ABB=ON  IMPEDANCE/CT
L168      16574 SEA FILE=EMBASE ABB=ON  ELECTRODE+NT/CT
L172       4570 SEA FILE=EMBASE ABB=ON  HIGH(W)(RESIST? OR THROUGH?)
L174        316 SEA FILE=EMBASE ABB=ON  (L140 OR L163 OR L164) AND L165 AND
                ((L166 OR L167 OR L168))
L176          2 SEA FILE=EMBASE ABB=ON  L172 AND L174


L139       3475 SEA FILE=EMBASE ABB=ON  APPARATUS/CT
L140      28510 SEA FILE=EMBASE ABB=ON  ION CHANNEL+NT/CT
L163      32883 SEA FILE=EMBASE ABB=ON  CALCIUM TRANSPORT/CT OR SODIUM
                TRANSPORT/CT OR CHLORIDE TRANSPORT/CT OR POTASSIUM TRANSPORT/CT

L164       9187 SEA FILE=EMBASE ABB=ON  ION TRANSPORT/CT
L165     455506 SEA FILE=EMBASE ABB=ON  MEMBRANE#
L166        916 SEA FILE=EMBASE ABB=ON  ELECTRIC RESISTANCE/CT
L167       3850 SEA FILE=EMBASE ABB=ON  IMPEDANCE/CT
L168      16574 SEA FILE=EMBASE ABB=ON  ELECTRODE+NT/CT
L174        316 SEA FILE=EMBASE ABB=ON  (L140 OR L163 OR L164) AND L165 AND
                ((L166 OR L167 OR L168))
L178          0 SEA FILE=EMBASE ABB=ON  L139 AND L174


L214          9 (L177 OR L175 OR L176)

=> dup rem l211,l209,l212,l213,l214,l210
FILE 'MEDLINE' ENTERED AT 17:04:07 ON 24 APR 2002

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FILE 'WPIDS' ENTERED AT 17:04:07 ON 24 APR 2002
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PROCESSING COMPLETED FOR L211
PROCESSING COMPLETED FOR L209
PROCESSING COMPLETED FOR L212
PROCESSING COMPLETED FOR L213
PROCESSING COMPLETED FOR L214
PROCESSING COMPLETED FOR L210
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I215 61 DUP REM L211 L209 L212 L213 L214 L210 (2 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE MEDLINE
ANSWERS '7-32' FROM FILE CAPLUS
ANSWERS '33-43' FROM FILE BIOSIS
ANSWERS '44-45' FROM FILE BIOTECHNO
ANSWERS '46-53' FROM FILE EMBASE
ANSWERS '54-61' FROM FILE WPIDS

=> d ibib ab 1-61; fil hom

L215 ANSWER 1 OF 61 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 95019641 MEDLINE
DOCUMENT NUMBER: 95019641 PubMed ID: 7934029
TITLE: Applications of electrophysiology in studies of ion transport by gut mucosa.
AUTHOR: Soybel D I
CORPORATE SOURCE: Department of Surgery, Brigham and Women's Hospital, Boston, Massachusetts 02115.
CONTRACT NUMBER: R29 DK44571 (NIDDK)
SOURCE: JOURNAL OF SURGICAL RESEARCH, (1994 Oct) 57 (4) 510-26.
Ref: 41
Journal code: K7B; 0376340. ISSN: 0022-4804.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941107

L215 ANSWER 2 OF 61 MEDLINE
ACCESSION NUMBER: 2001229803 MEDLINE
DOCUMENT NUMBER: 21219871 PubMed ID: 11322529
TITLE: The effects of interpulse interval on stochastic properties of electrical stimulation: models and measurements.
AUTHOR: Matsuoka A J; Rubinstein J T; Abbas P J; Miller C A
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, The University of Iowa, Iowa City 52242, USA..
hiro@earpower.oto.uiowa.edu
CONTRACT NUMBER: DC-6-2111 (NIDCD)
DC/OD-0-2948 (NIDCD)
SOURCE: IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, (2001 Apr) 48 (4) 416-24.
Journal code: GFX; 0012737. ISSN: 0018-9294.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517
AB It is known that some cochlear implant users have improved speech perception using higher rates of interleaved pulsatile stimulation. There are, however, significant limitations on their performance presumably due in part to temporal and spatial interactions. To address these limitations, we have examined refractory characteristics of the auditory nerve using experimental animal models and computational simulations. A stochastic model of the node of Ranvier modified for mammalian sodium channel kinetics has been developed to calculate the masked input-output

(I/O) functions for different interpulse intervals (IPI) [26]. The model is based upon 1000 voltage-gated sodium channels and incorporates parameters such as nodal resistance and capacitance. The relative spread (RS) [35] calculated from the I/O functions was typically 0.03 for 17 different IPIs between 450 micros and 6 ms for cathodal stimuli. For IPI = 830 and 870 micros, the RS was ten times greater than those for other IPIs. Although it is not fully understood how the electrically evoked compound action potential (EAP) data are related to single fiber data, the RS of single fibers is a partial contributor [19]. We have measured the EAP using a monopolar intracochlear stimulating electrode and a recording electrode placed directly on the nerve and have observed changes in slope of EAP growth functions consistent with the theoretical RS values. These results have significant implications for speech coding in a cochlear implant since they suggest an increased membrane noise for pulse trains of specific rates.

L215 ANSWER 3 OF 61 MEDLINE
ACCESSION NUMBER: 2001645868 MEDLINE
DOCUMENT NUMBER: 21554970 PubMed ID: 11698075
TITLE: 3H]dofetilide binding to HERG transfected membranes: a potential **high throughput** preclinical screen.
AUTHOR: Finlayson K; Turnbull L; January C T; Sharkey J; Kelly J S
CORPORATE SOURCE: Fujisawa Institute of Neuroscience, University of Edinburgh, 1 George Square, EH8 9JZ, Edinburgh, UK.. Keith.Finlayson@ed.ac.uk
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (2001 Oct 26) 430 (1) 147-8.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011108
Last Updated on STN: 20020125
Entered Medline: 20020103

AB The pharmacological characteristics of [3H]dofetilide binding were examined in membranes prepared from human embryonic kidney (HEK293) cells stably expressing human ether-a-go-go related gene (HERG) K+ channels. The classIII antiarrhythmic compounds dofetilide, clofilium, 4'-[[1-[2-(6-methyl-2-pyridyl)ethyl]-4-piperidyl]carbonyl]methanesulfonanilide (E-4031), N-methyl-N-[2-[methyl-(1-methyl-1H-benzimidazol-2-yl)amino]ethyl]-4-[(methylsulfonyl)amino]benzene-sulfonamide (WAY-123,398) and d-sotalol all inhibited [3H]dofetilide binding. In addition, the structurally unrelated compounds pimozide, terfenadine and haloperidol, all of which prolong the QT interval in man, also inhibited binding. These data indicate that a [3H]dofetilide binding assay using HERG membranes may help identify compounds that prolong the QT interval.

L215 ANSWER 4 OF 61 MEDLINE
ACCESSION NUMBER: 2001438448 MEDLINE
DOCUMENT NUMBER: 21377020 PubMed ID: 11484792
TITLE: The identification of the sympathetic neurons innervating the hamster submandibular gland and their electrophysiological membrane properties.
AUTHOR: Morita M; Suzuki T
CORPORATE SOURCE: Department of Physiology, Tokyo Dental College, Chiba, Japan.
SOURCE: BULLETIN OF TOKYO DENTAL COLLEGE, (2001 Feb) 42 (1) 15-33.
Journal code: C6E; 7505414. ISSN: 0040-8891.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB The neuron innervating the hamster submandibular (SM) gland was identified in the superior cervical ganglion (SCG) in vitro by recording the antidromic response using the intracellular recording technique. After the cellular response was recorded, methylene blue was injected iontophoretically into the neuron from the recording electrode, and the location of the cell soma was determined. The salivatory neurons of the SM gland were in the small- to medium-sized group of the entire cell population of the SCG. The cell size was 36.3 x 24.4 microm (mean, n=45). The postganglionic fibers were entirely unmyelinated (mean: 0.34 m/sec at 28-30 degrees C, n=141). Eighty-seven percent of the cells were distributed in the central one-third of area between the external carotid nerve origin and the caudal pole in the SCG. The resting membrane potential, membrane input resistance, membrane time constant and membrane input capacitance of the salivatory neuron were as follows: -49.2+/-7.6 mV (n=102), 52.9+/-23.6 Mohms (n=71), 8.0+/-3.4 msec (n=71) and 147+/-50 pF (n=71). Fast- and slow-excitatory postsynaptic potentials (EPSPs) were evoked, but not slow-inhibitory postsynaptic potentials (IPSPs). The fast EPSP was 13.1+/-5.7 mV in amplitude and 46.2+/-17.1 msec in duration (n=35). The slow EPSP (20 Hz, 5 sec) was 6.9+/-11 .9 mV in amplitude and 101+/-43 sec in duration (n=16). The directly-evoked spike was 63.0+/-11.9 mV in amplitude and 5.9+/-1.3 msec in duration (n=54). The spike after-hyperpolarization (AHP) was 12.5+/-3.5 mV in amplitude and 353+/-161 msec in duration. Na+ and Ca+ channels were involved in the spike generation. The voltage-dependent K+ channels (delayed rectifier), A channels and rapidly Ca2+-activated K+ channels (BK channels) regulated the spike-falling phase. The delayed rectifiers, A channels, and BK and SK (slowly Ca2+-activated) channels were involved in generation of spike-AHP. Muscarine suppressed the Ca2+ component of spike via muscarinic receptors.

L215 ANSWER 5 OF 61 MEDLINE
ACCESSION NUMBER: 1999190759 MEDLINE
DOCUMENT NUMBER: 99190759 PubMed ID: 10089572
TITLE: Microelectrode measurements of the effects of basolateral adenosine in polarized human intestinal epithelial cells in culture.
AUTHOR: Bouritius H; Bajnath R B; Groot J A
CORPORATE SOURCE: Graduate School for the Neurosciences, Institute of Neurobiology, Faculty of Biology, University of Amsterdam, Kruislaan 320, 1098 SM Amsterdam, The Netherlands.
SOURCE: PFLUGERS ARCHIV. EUROPEAN JOURNAL OF PHYSIOLOGY, (1999 Mar) 437 (4) 589-95.
Journal code: OZX; 0154720. ISSN: 0031-6768.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990511
Last Updated on STN: 19990511
Entered Medline: 19990423

AB Activation of the basolateral receptor for adenosine in HT-29cl.19A cells, by 100 microM adenosine, increased the equivalent short-circuit current (DeltaIsc= 24+/-2 microA/cm2), depolarized the intracellular potential (DeltaVa= 26+/-2 mV) and decreased the fractional apical membrane resistance (DeltafRa=-0.48). The changes in all parameters reached their peak values simultaneously. This suggests that the primary action of the adenosine-activated pathway is on only one membrane. Bumetanide inhibited

the transepithelial response and repolarized the cell potential. After preincubation with 100 microM forskolin, application of 300 microM adenosine caused a significant further change in Va, Isc, the transepithelial potential (Vt) and fRa. Together with the results from ion-replacement studies, the observations indicate that adenosine activates channels other than the cystic fibrosis transmembrane conductance regulator (CFTR). The rank order of potencies of adenosine and adenosine analogues implies that the receptor is of the A2 subtype. Preincubation with 4-bromophenacyl bromide (4-BPB) inhibited the effect of an adenosine analogue by 50%, indicating that activation of phospholipase A2 may be involved in the adenosine-induced response.

L215 ANSWER 6 OF 61 MEDLINE
ACCESSION NUMBER: 95216757 MEDLINE
DOCUMENT NUMBER: 95216757 PubMed ID: 7702191
TITLE: Biomagnetic neurosensors. 3. Noninvasive sensors using magnetic stimulation and biomagnetic detection.
AUTHOR: Babb C W; Coon D R; Rechnitz G A
CORPORATE SOURCE: Hawaii Biosensor Laboratory, Department of Chemistry, University of Hawaii, Honolulu 96822.
SOURCE: ANALYTICAL CHEMISTRY, (1995 Feb 15) 67 (4) 763-9. Journal code: 4NR; 0370536. ISSN: 0003-2700.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19990129
Entered Medline: 19950502

AB A noninvasive biomagnetic sensor system that uses magnetic toroids for both neural stimulation and detection is described. It is shown that analytical signals obtained by direct magnetic detection (no signal averaging) compare favorably with electrical monitoring and that dose-response curves for local anesthetics correlate well between the two methods. Neural lifetimes are significantly extended when the noninvasive biomagnetic sensing system is used.

L215 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:598288 CAPLUS
DOCUMENT NUMBER: 135:164434
TITLE: Planar patch clamp electrodes
INVENTOR(S): Klemic, Kathryn C.; Klemic, James F.; Reed, Mark A.; Sigworth, Frederick J.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059447	A1	20010816	WO 2001-US4407	20010212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-181935P P 20000211
AB The present invention relates to ionic electrodes, particularly microelectrodes and electrode arrays, and also relates to fabrication methods for such electrodes. In particular, the present invention relates to planar polymer electrodes for making patch clamp measurements of ionic currents through biol. membranes, such as the plasma membranes of living cells. The electrodes of the present invention are useful for measuring individual and multisite cell membrane currents and voltages, as well as in **high-throughput** screening procedures.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123543 CAPLUS
DOCUMENT NUMBER: 136:163683
TITLE: Arrays of biological membranes and methods and use thereof
INVENTOR(S): Lahiri, Joydeep; Fang, Ye; Jonas, Steven J.; Kalal, Peter J.; Wang, Wei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002019015	A1	20020214	US 2001-854786	20010514

PRIORITY APPLN. INFO.: US 2000-224135P P 20000810
AB The present invention overcomes the problems and disadvantages assocd. with prior art arrays by providing an array comprising a plurality of biol. membrane microspots assocd. with a surface of a substrate that can be produced, used and stored, not in an aq. environment, but in an environment exposed to air under ambient or controlled humidities. Preferably, the biol. membrane microspots comprise a membrane bound protein. Most preferably, the membrane bound protein is a G-protein coupled receptor, an ion channel or a receptor tyrosine kinase.

L215 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798300 CAPLUS
DOCUMENT NUMBER: 135:341127
TITLE: Use of secondary cell wall proteins of procaryotic microorganisms
INVENTOR(S): Sleytr, Uwe B.; Sara, Margit; Mader, Christoph; Schuster, Bernhard; Unger, Frank M.
PATENT ASSIGNEE(S): Austria
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081425	A1	20011101	WO 2001-AT122	20010424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: AT 2000-732 A 20000426
AB The invention concerns the use of a secondary cell wall proteins (SCWP) for oriented monomol. binding of mol. layers and/or addn. of mols. of a carrier. The invention also concerns the prodn. of composite layers. Secondary cell wall polymers can be modified and used on ultrafiltration membranes or silica waffles as connecting layers for S-layer proteins, lipids, vesicles etc. The obtained multilayers are used e.g. for **high throughput** screening, drug screening, diagnostic agents. Thus SCWP were isolated from the sacculi of various Bacillaceae using hydrogen fluoride, gel chromatog., dialysis and lyophilization. SCWP were modified in several procedures, e.g. conversion of the aldehyde group into amino group; formation of thiol group; biotinylation. SCWP were also reacted with DPPE to form glycolipids; glycolipids were used to produced liposomes for the oriented binding of S-layer proteins.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:713653 CAPLUS
DOCUMENT NUMBER: 135:254073
TITLE: New apparatus and method for electrophysiological testing of biological membranes.
INVENTOR(S): Trumbull, Jonathan D.; Bertrand, Daniel C.; Briggs, Clark A.; Mckenna, David G.; Maslana, Eugene S.; Blanchard, David P.; Pan, Jeffrey Y.; Bojan, Peter M.; Nemcek, Thomas A.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071312	A2	20010927	WO 2001-US9110	20010321

W: AU, CA, JP, MX, NO
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
PRIORITY APPLN. INFO.: US 2000-532686 A 20000322
US 2001-790871 A 20010223
AB The invention concerns a method and app. for running a plurality of tests concurrently to obtain data relating to the electrophysiol. properties of receptors and channels in biol. membranes of test subjects, such as, for example, Xenopus oocytes. The invention further provides software for controlling, acquiring, and recording data relating to electrophysiol. properties of receptors and channels in biol. membranes of test subjects, such as, for example, oocytes. This invention increases the throughput rate for expts. and assays employing receptors and ion channels expressed in biol. membranes of test subjects, such as, for example, oocytes. In the case of an oocyte, these receptors and channels may be natively expressed (endogenous), may be placed into the oocyte (exogenous), or may be expressed from other RNA or DNA previously placed into the oocyte (exogenous). The invention provides a means for a sole researcher to operate a plurality of electrophysiol. test stations in the time and space conventionally required by a single electrophysiol. test station. The invention automates these stations and provides a means for a sole

individual to perform large sets of expts. that would be phys. and mentally exhausting in the absence of this invention. In addn., this invention provides efficient database and data anal. software integrated with the data acquisition software, thereby increasing the user's data-handling productivity to keep pace with the augmented data generation capacity. Diagrams describing the app. are given.

L215 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:338854 CAPLUS
DOCUMENT NUMBER: 134:350285
TITLE: Ion channel permeability
INVENTOR(S): Castle, Neil; Ford, John
PATENT ASSIGNEE(S): Cambridge Drug Discovery Limited, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001033219	A2	20010510	WO 2000-GB4185	20001102
WO 2001033219	A3	20020314		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-25799 A 19991102
AB Methods for identifying modulators of ion channel permeability are described which comprise: (a) providing an ion channel in the presence and absence of a candidate modulator of the permeability of the ion channel; (b) providing a fluorescent dye (such as MEQ, SPQ, or LZQ) and halide ions, which act as a fluorescence quencher, on a first side of the ion channel; (c) providing thallium ions on a second side of the ion channel which ppt. the halide ions when they are caused or allowed by the ion channel to pass from the second to the first side of the ion channel, thereby relieving fluorescence quenching by the halide ions; and (d) comparing any change in the fluorescence signal in the absence of the candidate modulator with any change in the fluorescence signal in the presence of the candidate modulator. Such methods are particularly suited for **high throughput** screening of candidate modulators of ion channel permeability. Methods for observing and assaying for ion channel permeability are also described.

L215 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:31628 CAPLUS
DOCUMENT NUMBER: 134:96212
TITLE: Virus like particles, their preparation and their use preferably in pharmaceutical screening and functional genomics
INVENTOR(S): Hunt, Nicholas
PATENT ASSIGNEE(S): Evotec Biosystems A.-G., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002551	A2	20010111	WO 2000-EP6144	20000626
WO 2001002551	A3	20011108		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1187928	A2	20020320	EP 2000-949236	20000630

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

EP 1999-112451	A	19990630
US 1999-141268P	P	19990630
EP 2000-106109	A	20000321
EP 2000-110363	A	20000515
WO 2000-EP6144	W	20000626

AB The invention relates to virus like particles (VLP), their prepn. and their use in pharmaceutical screening and functional genomics. The VLP can display the target protein within the its capsid through either strong specific interaction of a mol. peptide tag covalently attached to the C-terminus of the signal protein (Gag) with a complementary specific peptide tag assocd. with the target of interest or by direct covalent fusion of the Gag protein with the target protein/peptide of interest. The Gag-tag fusion protein is co-expressed in a cellular system with the resp. mol. of interest which also carries a specific peptide tag either within the mol. or at either the N- or C-terminus. Expression of the modified Gag protein in the resp. host cells results in the accumulation of the Gag protein at the plasma membrane due to signals present within the N-terminal portion of the Gag protein. High concns. of this protein at the plasma membrane results in a budding process in which VLPs are released into the extracellular milieu. If the target protein carrying the complementary tag is expressed in the same cell and is concd. in the intracellular compartments then the specific interaction with the tagged Gag protein results in the cotransport of the target to the plasma membrane and subsequent incorporation into the released VLPs. The invention further provides a variety of assay formats to be used with said virus like particles. The invention is exemplified by displaying G-protein coupled receptors, or human epidermal growth factor receptor (EGFR), or endothelin receptors to allow identification of gene products interfering with protein-protein interactions within the cell.

L215 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:885303 CAPLUS
DOCUMENT NUMBER: 136:577
TITLE: Sensor electrode apparatus for the amperometric and/or potentiometric testing of especially pharmacological sites of activity and active substances
PATENT ASSIGNEE(S): Iongate Biosciences G.m.b.H., Germany
SOURCE: Ger. Gebrauchsmusterschrift, 48 pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 20104431	U1	20011206	DE 2001-20104431	20010315

AB The invention discloses a sensor electrode app., in particular for a biosensor device or the like, for the amperometric and/or potentiometric testing of esp. pharmacol. sites of action and/or active substances. Schematic diagrams of the app. are included.

L215 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:467980 CAPLUS
DOCUMENT NUMBER: 135:43098
TITLE: Method for the preparation of **biosensors** composed of ion channels embedded in lipid bilayers
INVENTOR(S): Friedrich, Steffen; Salzer, Reiner; Herzog, Klaus
PATENT ASSIGNEE(S): Technische Universitaet Dresden, Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19961951	A1	20010628	DE 1999-19961951	19991220

AB The invention concerns the prepn. of ion channel contg. lipid bilayers as biosensors for applications. g. in drug screening, testing of food toxins. Polyester membranes (1-30 .mu.m) are punched with ion beam and etching; the holes (2-10 .mu.m) are filled with lipids to form a bilayer and ion channels are integrated into the lipid bilayer. Lipid layers are formed from a squalene soln. using pasting or Langmuir-Blodgett method; nicotinic acetylcholine receptors are the ion channels. Squalen is biocompatible and at temps. of the measurements the openings of the ion channels are optimized. Fluid reservoirs are on both sides of the membrane with immersed electrodes; for measuring ion, flux radiotracers are incorporated. The unit is provided with microinjectors and a microscope cover slip for microscopic detection. A device for measurement with such biosensory layers is described.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:875312 CAPLUS
DOCUMENT NUMBER: 136:228567
TITLE: Deposition of highly resistive lipid bilayer on silicon-silicon dioxide electrode and incorporation of gramicidin studied by ac impedance spectroscopy
AUTHOR(S): Purrucker, Oliver; Hillebrandt, Heiko; Adlkofer, Klaus; Tanaka, Motomu
CORPORATE SOURCE: Lehrstuhl fur Biophysik E22, Technische Universitat Munchen, Garching, D-85748, Germany
SOURCE: Electrochimica Acta (2001), 47(5), 791-798
CODEN: ELCAAV; ISSN: 0013-4686
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Highly resistive planar supported lipid membranes were deposited onto highly doped p-type silicon-silicon dioxide electrodes. Phys. parameters of the substrates (e.g. dopant, doping ratio and oxide layer thickness) were optimized by a combined study using ellipsometry and ac impedance spectroscopy. Lipid bilayer was deposited by fusion of small unilamellar vesicles, and the self-assembling of the homogeneous bilayer could be monitored as a function of time. Impedance spectroscopy over a wide frequency range (from 20 kHz to 10 mHz) enables sepg. membrane resistance

and capacitance from the background signals. Membrane resistance amounted to 1.0 M.OMEGA. Cm2, and the capacitance was around 0.7 .mu.F cm-2. The resistance obtained here is comparable to that of the freestanding black lipid membrane. Although the area of the supported membrane (0.5 Cm2) is much larger than that of the black lipid membrane (.apprx.0.002 Cm2), the elec. properties were stable for more than a week. Gramicidin D was inserted into the membrane from trifluoroethanol soln., and activity of the channels was checked in terms of membrane conductance and ion selectivity. Functional incorporation of ion channels into the supported membrane demonstrated here suggested that the gramicidin monomers could diffuse over the membranes to form transmembrane pores.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:231037 CAPLUS
DOCUMENT NUMBER: 134:275973
TITLE: Vasopressin regulates water flow in a rat cortical collecting duct cell line not containing known aquaporins
AUTHOR(S): Capurro, C.; Rivarola, V.; Kierbel, A.; Escoubet, B.; Farman, N.; Blot-Chabaud, M.; Parisi, M.
CORPORATE SOURCE: Laboratorio de Biomembranas. Dpto de Fisiologia, Facultad de Medicina, Univ. de Buenos Aires, Argent.
SOURCE: Journal of Membrane Biology (2001), 179(1), 63-70
CODEN: JMBBBO; ISSN: 0022-2631
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Transepithelial** water movements and arginine-vasopressin (AVP)-assocd. ones were studied in a renal cell line established from a rat cortical collecting duct (RCCD1). **Transepithelial** net water fluxes (Jw) were recorded every minute in RCCD1 monolayers cultured on permeable supports. Spontaneous net water secretion was obsd., which was inhibited by serosal bumetanide (10-5 M), apical glibenclamide (10-4 M) and apical BaCl2 (5 .times. 10-3 M). RT-PCR, RNAse protection and/or immunoblotting expts. demonstrated that known renal aquaporins (AQP1, AQP2, AQP3, AQP4, AQP6 and AQP7) were not expressed in RCCD1 cells. AVP stimulates cAMP prodn. and sodium resorption in RCCD1 cells. The authors have now obsd. that AVP significantly reduces the spontaneous water secretory flux. The amiloride-sensitive AVP-induced increase in short-circuit current (Isc) was paralleled by a simultaneous modification of the obsd. Jw: both responses had similar time courses and half-times (about 4 min). On the other hand, AVP did not modify the osmotically driven Jw induced by serosal hypertonicity. The authors can conclude that: **transepithelial** Jw occurs in RCCD1 cells in the absence of known renal aquaporins; the "water secretory component" obsd. could be linked to Cl- and K+ secretion; the natriferic response to AVP, preserved in RCCD1 cells, was assocd. with a change in net water flux, which was even obsd. in absence of AQP2, AQP3 or AQP4; and the hydro-osmotic response to AVP was completely lost.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:609025 CAPLUS
DOCUMENT NUMBER: 133:174245
TITLE: Minimally invasive apparatus and method for testing lesions of the oral cavity and similar epithelium
INVENTOR(S): Eisen, Drore; Frist, Stephen; Recht, Joel
PATENT ASSIGNEE(S): Oralscan Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051066	A1	20000831	WO 2000-US743	20000112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6284482	B1	20010904	US 1999-298218	19990423
EP 1155381	A1	20011121	EP 2000-902395	20000112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-121255P P 19990223
US 1999-298218 A 19990423
US 1999-298219 A 19990423
WO 2000-US743 W 20000112

AB A sample of an epithelial lesion which may be keratinized is disclosed in which an anal. system including an imaging system is provided to detect precancerous and cancerous cells. A **transepithelial** non-lacerational brush produces sufficient cells from all three layers of the epithelium so that an anal. system comprising a programmed computer can detect which cells exhibit abnormal keratinization and require further examn. because of a likely suspicion of said pre-cancerous and cancerous conditions. The method and system can apply to the diagnosis of non-cancerous conditions as well.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:291355 CAPLUS
DOCUMENT NUMBER: 132:319478
TITLE: Biological ion channels in nanofabricated detectors
INVENTOR(S): McGeoch, Julie E. M.; McGeoch, Malcolm W.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025121	A1	20000504	WO 1999-US24043	19991022
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1125120	A1	20010822	EP 1999-971087	19991022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002006357	A1	20020117	US 2001-844516	20010427

PRIORITY APPLN. INFO.:
US 1998-105842P P 19981027
US 1999-140111P P 19990618
WO 1999-US24043 W 19991022

AB The present invention relates to a device for generating an oscillating elec. current, where the device incorporates an ion channel. In particular, the ion channel is incorporated into an integrated electronic device having nanoscale dimensions. Thus, this device can transform biol. processes into an elec. output. The present invention also describes a sensor for detecting biol. or chem. analytes with the ion channel device. Methods for generating the oscillating currents and detecting the analytes are also disclosed.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:810938 CAPLUS
DOCUMENT NUMBER: 134:112505
TITLE: Ion Channel Behavior of Supported Bilayer Lipid Membranes on a Glassy Carbon Electrode
AUTHOR(S): Wu, Zhengyan; Tang, Jilin; Cheng, Zhiliang; Yang, Xiurong; Wang, Erkang
CORPORATE SOURCE: Laboratory of Electroanalytical Chemistry and National Analytical Research Center of Electrochemistry and Spectroscopy Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun Jilin, 130022, Peop. Rep. China
SOURCE: Analytical Chemistry (2000), 72(24), 6030-6033
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new kind of solid substrate, a glassy carbon (GC) electrode, was selected to support lipid layer membranes. On the surface of the GC electrode, we made layers of didodecyldimethylammonium bromide (a synthetic lipid). From electrochem. impedance expts., we demonstrated that the lipid layers on the GC electrode were bilayer lipid membranes. We studied the ion channel behavior of the supported bilayer lipid membrane. In the presence of perchlorate anions as the stimulus and ruthenium(II) complex cations as the marker ions, the lipid membrane channel was open and exhibited distinct channel current. The channel was in a closed state in the absence of perchlorate anions.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:714511 CAPLUS
DOCUMENT NUMBER: 132:32015
TITLE: Formation of anion-selective channels in the cell plasma membrane by the toxin VacA of Helicobacter pylori is required for its biological activity
AUTHOR(S): Szabo, Ildiko; Brutsche, Sandra; Tombola, Francesco; Moschioni, Monica; Satin, Barbara; Telford, John L.; Rappuoli, Rino; Montecucco, Cesare; Papini, Emanuele; Zoratti, Mario
CORPORATE SOURCE: Centro CNR Biomembrane e Dipartimento di Scienze Biomediche, Universita di Padova, Padua, 35121, Italy
SOURCE: EMBO Journal (1999), 18(20), 5517-5527
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vacuolating toxin VacA, a major determinant of Helicobacter pylori-assocd. gastric diseases, forms anion-selective channels in artificial planar lipid bilayers. Here we show that VacA increases the anion permeability of the HeLa cell plasma membrane and dets. membrane depolarization. Electrophysiol. and pharmacol. approaches indicated that

this effect is due to the formation of low-conductance VacA pores in the cell plasma membrane and not to the opening of Ca2+- or vol.-activated chloride channels. VacA-dependent increase of current conduction both in artificial planar lipid bilayers and in the cellular system was effectively inhibited by the chloride channel blocker 5-nitro-2-(3-phenylpropylamino) benzoic acid (NPPB), while 2-[(2-cyclopentenyl-6,7-dichloro-2,3-dihydro-2-methyl-1-oxo-1H-inden-5- yl)oxy] acetic acid (IAA-94) was less effective. NPPB inhibited and partially reversed the vacuolation of HeLa cells and the increase of ion cond. of polarized Madine Darby canine kidney cell monolayers induced by VacA, while IAA-94 had a weaker effect. We conclude that pore formation by VacA accounts for plasma membrane permeabilization and is required for both cell vacuolation and increase of **trans-epithelial** cond.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:765944 CAPLUS
DOCUMENT NUMBER: 132:90203
TITLE: The peptide-tethered lipid membrane as a biomimetic system to incorporate cytochrome c oxidase in a functionally active form
AUTHOR(S): Naumann, R.; Schmidt, E. K.; Jonczyk, A.; Fendler, K.; Kadenbach, B.; Liebermann, T.; Offenhausser, A.; Knoll, W.
CORPORATE SOURCE: Max Planck Institute of Polymer Research, Mainz, D-55128, Germany
SOURCE: Biosensors & Bioelectronics (1999), 14(7), 651-662
CODEN: BBIOE4; ISSN: 0956-5663
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptide-supported lipid bilayers are investigated as a new class of solid supported membranes tethered to the support by a peptide spacer. They are referred to as peptide tethered lipid membranes (tBLMs), formed by the fusion of liposomes with a thiopeptide-lipid monolayer chemisorbed on a gold support. Peptide tBLMs are designed as a biomimetic system to investigate integral membrane proteins. As an example, cytochrome c oxidase (COX) from bovine heart is incorporated into the preformed peptide tBLM by diln. of the solubilized protein below the crit. micellar concn. The formation of the lipid film as well as the incorporation of the protein were monitored by surface plasmon resonance spectroscopy and surface plasmon fluorescence spectroscopy. COX is activated by adding the reduced form of cytochrome c to the air-satd. buffer soln. Using electrochem. techniques, such as square wave voltammetry (SWV) and chronoamperometry (CA), the direct electron transfer between COX and the gold electrode is obsd. as well as proton transport from the inside to the outside across the lipid bilayer. Proton transport is then further investigated using impedance spectroscopy, although the electrode is shown to be only partially (70%) covered with a bilayer while defect domains with only a monolayer of peptide or peptide-lipid coexist (approx. 30%). Proton transport carried out by the COX is shown to be voltage dependent. This transport is indicated as a resistance in parallel to the resistance of the lipid film. As a consequence, the total resistance decreases as a function of the concn. of cytochrome c and increases again either by removal of the substrate or by addn. of cyanide as an inhibitor of COX. The conductance in the presence of the activated enzyme correlates with the known turnover rate of COX. These expts. demonstrate the possibility to assess the activity of integral membrane proteins incorporated in peptide tBLMs using electrochem. techniques. The system could thus be promising for screening as well as biosensor applications.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:546858 CAPLUS
DOCUMENT NUMBER: 131:266702
TITLE: The effect of cis-diamminedichloroplatinum II on Na+ and K+, transport in the rabbit cortical collecting duct
AUTHOR(S): Susumu, Ookawara; Kaoru, Tabei; Hiroaki, Furuya; Yasushi, Asano
CORPORATE SOURCE: Division of Nephrology, Department of Internal Medicine, Jichi Medical School, Tochigi, Japan
SOURCE: Eur. J. Pharmacol. (1999), 378(1), 63-68
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cis-Dianuninedichloroplatinum II (CDDP) is an antineoplastic drug against solid malignant tumors. However, its clin. use is limited by nephrotoxicity. CDDP also causes hypokalemia and in vivo microperfusion method have demonstrated that luminal CDDP increases K+ secretion by hyperpolarization of the **transepithelial** voltage difference through stimulating Na+ transport in the distal segments. However, there is no direct evidence for this mechanism. We therefore examd. the effect of luminal CDDP on Na+ and K+ transport in the rabbit cortical collecting duct (CCD) using in vitro isolated tubular microperfusion. Luminal CDDP hyperpolarized the **transepithelial** voltage difference (VT) in a dose-dependent manner at concns. from 10-5 M to 10-3 M and at 10-3 M CDDP, VT was hyperpolarized from -11.6 .+-. 2.3 mV to -16.6 3.3 mV ($P < 0.001$). A concn. of 10-5 M ouabain. 10-4 M amiloride and 2 mM BaCl2 all completely abolished CDDP-induced hyperpolarization. To confirm the mechanism, Na4 and K+ flux were measured in the presence of 10-3 M CDDP. CDDP decreased net K+ secretion from -22.2 .+-. 5.7 to -15.2 .+-. 2.9 pmol mm-1 min-1 $P <$ 0.01) without any effect on the lumen-to-bath isotope flux of Na+ (52.6 .+-. 10.6 to 52.1 .+-. 10.7 pmol mm-1 min-1). These data suggest that luminal CDDP hyperpolarizes VT primarily by inhibiting K+ conductance but did not influence Na+ transport of the luminal membrane. We conclude that the CCD does not play a role in CDDP-induced hypokalemia when CDDP is applied from the luminal side.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L215 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:401847 CAPLUS
DOCUMENT NUMBER: 125:52989
TITLE: Biorecognition-controlled, ion-flow-modulating **biosensor**
INVENTOR(S): Pittner, Fritz; Schalkhammer, Thomas
PATENT ASSIGNEE(S): Austria
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612957	A1	19960502	WO 1995-AT197	19951011
W: US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AT 9401970	A	19970215	AT 1994-1970	19941019
AT 402935	B	19970925		
EP 734528	A1	19961002	EP 1995-933226	19951011

R: AT, CH, DE, FR, GB, LI
PRIORITY APPLN. INFO.: AT 1994-1970 19941019
WO 1995-AT197 19951011

AB This proposal is for a novel, highly sensitive sensor principle, the biorecognition-controlled, ion-flow-modulating biosensor with theor. sensitivity of a single analyte mol., which makes use of the binding of effector mols. (such effector mols. being any that bind to a ligand from the group consisting of hormones, peptides, enzyme inhibitors, environmental toxins, active pharmaceutical agents, thiols or chelate formers) to a ligand for the on/off control of an ion channel in a membrane. Suggested uses of the new biosensors are as blood HIV antibody sensors for HIV diagnosis and for monitoring HIV infection as well as urine estrogen sensors for ovulation detection.

L215 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:443737 CAPLUS
DOCUMENT NUMBER: 119:43737
TITLE: Trinitrophenyl-ATP blocks colonic chloride channels in planar phospholipid bilayers: evidence for two nucleotide binding sites
AUTHOR(S): Venglarik, Charles J.; Singh, Ashvani K.; Wang, Ruoping; Bridges, Robert J.
CORPORATE SOURCE: Gregory Fleming James Cystic Fibrosis Res. Cent., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: J. Gen. Physiol. (1993), 101(4), 545-69
CODEN: JGPLAD; ISSN: 0022-1295
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Outwardly rectifying 30-50-pS Cl- channels mediate cell vol. regulation and **transepithelial** transport. Several recent reports indicate that rectifying Cl- channels are blocked after addn. of ATP to the extracellular bath (Alton, E. W. F. W. et al., 1991 Paulmichl, M., Y. et al., 1992). Therefore, the authors decided to conduct a more detailed study of the ATP binding site using a higher affinity probe. The authors tested the ATP deriv., 2',3',O-(2,4,6-trinitrocyclohexadienylidene) ATP (TNP-ATP), which has a high affinity for certain nucleotide binding sites. Here they report that TNP-ATP blocked colonic Cl- channels when added to either bath and that blockade was consistent with the closed-open-blocked kinetic model. The TNP-ATP concn. required for a 50% decrease in open probability was 0.27 .mu.M from the extracellular (cis) side and 20 .mu.M from the cytoplasmic (trans) side. Comparison of the off rate consts. revealed that TNP-ATP remained bound 28 times longer when added to the extracellular side compared with the cytoplasmic side. The authors performed competition studies to det. if TNP-ATP binds to the same sites as ATP. Addn. of ATP to the same bath contg. TNP-ATP reduced channel amplitude and increased the time the channel spent in the open and fast-blocked states (i.e., burst duration). This is the result expected if TNP-ATP and ATP compete for block, presumably by binding to common sites. In contrast, addn. of ATP to the bath opposite to the side contg. TNP-ATP reduced amplitude but did not alter burst duration. This is the result expected if opposite-sided TNP-ATP and ATP bind to different sites. In summary, the authors have identified an ATP deriv. that has a nearly 10-fold higher affinity for reconstituted rectifying colonic Cl- channels than any previously reported blocker (Singh, A. K. et al., 1991). Thus, TNP-ATP should be useful in future studies of ion channel nucleotide binding sites and possibly in preliminary steps of ion channel protein purifn. In addn., the authors have obtained good evidence that there are at least two nucleotide binding sites located on opposite sides of the colonic Cl- channel and that occupancy of either site produces a blocked state.

L215 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:251277 CAPLUS

DOCUMENT NUMBER: 116:251277
TITLE: Establishment and control of artificial ion-conductive zones for lipid membrane **biosensor** development
AUTHOR(S): Nikolelis, Dimitrios P.; Krull, Ulrich J.
CORPORATE SOURCE: Dep. Chem., Univ. Toronto, Mississauga, ON, L5L 1C6, Can.
SOURCE: Anal. Chim. Acta (1992), 257(2), 239-45
CODEN: ACACAM; ISSN: 0003-2670
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A chem. sensor based on activation of a process that mimics the opening of biol. ion channels is described. The interaction of bilayer lipid membranes prepd. from mixts. of egg phosphatidylcholine and dipalmitoylphosphatidic acid with Ca2+ was studied. At concns. of the neg. charged acidic lipid <25%, the ion conduction decreased with an increase of Ca2+ concn. This was due to a decrease in the surface charge d. and potential, which was caused by the binding of the divalent cations to the membrane surface. At concns. of the charged lipid >25%, interaction with divalent cations resulted in a phase sepn. involving formation of conductive zones by the charged lipid constituent in the membrane structure, and the ion permeability and cond. increased as the concn. of Ca2+ in the bulk soln. increased. The cond. changes due to the presence of Ca2+ could be fully reversed by the addn. of EDTA.

L215 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:37513 CAPLUS
DOCUMENT NUMBER: 116:37513
TITLE: **Biosensors** with ion channel-containing liquid crystalline membranes
INVENTOR(S): Gitler, Carlos; Yuli, Itzhak
PATENT ASSIGNEE(S): Yeda Research and Development Co., Ltd., Israel
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 441120	A2	19910814	EP 1991-100198	19910108
EP 441120	A3	19920122		
EP 441120	B1	19951129		
EP 441120	B2	20020403		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 93020	A1	19950629	IL 1990-93020	19900109
CA 2033776	AA	19910710	CA 1991-2033776	19910108
AT 130938	E	19951215	AT 1991-100198	19910108
ES 2082867	T3	19960401	ES 1991-100198	19910108
AU 9169245	A1	19910711	AU 1991-69245	19910109
AU 625017	B2	19920625		
US 5204239	A	19930420	US 1991-638488	19910109
JP 06090736	A2	19940405	JP 1991-188434	19910109
JP 3213341	B2	20011002		

PRIORITY APPLN. INFO.: IL 1990-93020 A 19900109

AB Biosensors for qual. and quant. anal. comprise an amphipathic liq. cryst. membrane composed of a lipid bilayer attached to a recording electrode via bridging anchoring mols. The lipid bilayer is doped with biol. or synthetic ion channels and is in continuous contact with a bulk aq. medium on both its surfaces. The bridging anchoring mols. may contain a phospholipid moiety linked to a polyoxyalkylene chain terminated with a thiol or thioether residue. Thus, acetylcholine receptors were

incorporated into mixed micelles contg. phosphatidylethanolamine-N-ethylene-(oxyethylene)10-ethylene-mercaptan as bridging mol. (prepn. given), followed by attachment of the mixed micelles to a Au electrode. The basal activity obsd. with acetylcholine receptor-contg. membranes was somewhat higher than that obsd. without any added dopant. On addn. of acetylcholine to the medium bathing the outer surface of the bilayer attached to the electrode, the appearance of increased noise level and some discrete channel events with different activity levels were obsd.; the enhanced activity remained for 30 min. Also described are prepn. of a mellitin-derived peptide conjugated with a trinitrobenzene-contg. peptide and interaction of the conjugate with anti-trinitrobenzene monoclonal antibody and the Au electrode-attached bilayer.

L215 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:2969 CAPLUS
DOCUMENT NUMBER: 116:2969
TITLE: Ion channel sensors for glutamic acid
AUTHOR(S): Minami, Hirotsugu; Sugawara, Masao; Odashima, Kazunori; Umezawa, Yoshio; Uto, Masayuki; Michaelis, Elias K.; Kuwana, Theodore
CORPORATE SOURCE: Fac. Sci., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Anal. Chem. (1991), 63(23), 2787-95
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Coulometric biosensors using glutamate receptor (GluR) ion channel protein as a signal-amplifying sensory element that exploit the glutamate-triggered Na+ current through bilayer lipid membranes were fabricated. The formation of stable planar bilayer lipid membranes was achieved by applying the folding method across a small circular aperture bored through a thin polyimide Film. The multichannel-type sensing membranes, formed across an aperture of .apprx.120 .mu.m diam., contained >10 GluR proteins and showed L-glutamic acid triggered response as a composite of individual single-channel currents. The single-channel-type sensing membranes, formed across an aperture of .apprx.20 .mu.m diam., contained a sufficiently small no. of GluR proteins so that the response was obsd. as a series of single-channel pulse currents. Dependence of the integrated channel current on the glutamate concn. was examd. A sharp concn. dependence up to .apprx.1.5 .times. 10-7M and 3 .times. 10-6M for the multichannel single-channel type sensors, resp., was obsd. A high selectivity for L-glutamate compared with D-glutamate for inducing the channel current was obsd. A detection limit as low as .apprx.3 .times. 10-8M was attained for the multichannel-type sensor. This remarkable sensitivity is discussed in terms of the potential use of GluR ion channel protein for a new type of sensing system.

L215 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:653807 CAPLUS
DOCUMENT NUMBER: 115:253807
TITLE: Formation of ion-conducting channels by the membrane attack complex proteins of complement
AUTHOR(S): Shiver, John W.; Dankert, John R.; Esser, Alfred F.
CORPORATE SOURCE: Dep. Comp. Exp. Pathol., Univ. Florida, Gainesville, FL, 32610, USA
SOURCE: Biophys. J. (1991), 60(4), 761-9
CODEN: BIOJAU; ISSN: 0006-3495
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of sequential addns. of purified human complement proteins C5b-6, C7, C8, and C9 to assemble the C5b-9 membrane attack complex (MAC) of complement on elec. properties of planar lipid bilayers have been analyzed. The **high resistance** state of such membranes was impaired after assembly of large nos. of C5b-8 complexes as indicated

by the appearance of rapidly fluctuating membrane currents. The C5b-8 induced conductance was voltage dependent and rectifying at higher voltages. Addn. of C9 to membranes with very few C5b-8 complexes caused appearance of few discrete single channels of low conductance (5-25 pS) but after some time very large (>0.5 nS) jumps in conductance could be monitored. This high macroscopic conductance state was dominated by 125-pS channels having a lifetime of .apprx.1 s. The high conductance state was not stable and declined again after a period of 1-3 h. Incorporation of MAC extd. from complement-lysed erythrocytes into liposomes and subsequent transformation of such complexes into planar bilayers via an intermediate monolayer state resulted in channels with characteristics similar to the ones produced by sequential assembly of C5b-9. Comparison of the high-conductance C5b-9 channel characteristics (lifetime, ion preference, ionic-strength dependence) with those produced by poly(C9) (the circular or tubular aggregation product of C9) indicates that the two are significantly different.

L215 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:79572 CAPLUS
DOCUMENT NUMBER: 116:79572
TITLE: Control of **ion transport** through lipid membranes
AUTHOR(S): Krull, Ulrich; Nikolelis, Dimitrios P.; Brennan, John D.; Brown, R. Stephen; Thompson, Michael; Ghaemmaghami, Vida; Kallury, Krishna M.
CORPORATE SOURCE: Dep. Chem., Univ. Toronto, Mississauga, ON, L5L 1C6, Can.
SOURCE: Anal. Proc. (London) (1991), 28(11), 370-2
CODEN: ANPRDI; ISSN: 0144-557X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Progress towards a surface-stabilized a.c. admittance modulation lipid membrane-based biosensor that operates on the basis of control of ion permeation by artificial ion channels is described.

L215 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:115305 CAPLUS
DOCUMENT NUMBER: 112:115305
TITLE: Receptor membranes for bisensor devices
INVENTOR(S): Cornell, Bruce Andrew; Braach-Maksvytis, Vijoleta Lucija Bronislava
PATENT ASSIGNEE(S): Commonwealth Scientific and Industrial Research Organization, Australia
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8901159	A1	19890209	WO 1988-AU273	19880727
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8821279	A1	19890301	AU 1988-21279	19880727
AU 617687	B2	19911205		
EP 382736	A1	19900822	EP 1988-907164	19880727
EP 382736	B1	19941102		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03503209	T2	19910718	JP 1988-506329	19880727
CA 1335879	A1	19950613	CA 1988-573217	19880727
US 5436170	A	19950725	US 1990-473932	19900125

PRIORITY APPLN. INFO.: AU 1987-3346 19870727
AU 1987-3348 19870727
AU 1987-3453 19870731
AU 1987-4478 19870921
WO 1988-AU273 19880727

AB A membrane comprising a closely packed array of self-assembling amphiphilic mols. is characterized in that it incorporates ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. conjugated with a supporting entity. The ion channel is selected from peptides capable of forming helices and aggregates thereof, coronands, cryptands, podands, or combinations thereof. In the amphiphilic mols. comprising a receptor mol. conjugated with a supporting entity, the receptor mol. has a receptor site and is Igs, antibodies, antibody fragments, dyes, enzymes, or lectins. The supporting entity is a lipid head group, a hydrocarbon chain(s), a cross-linkable mol., or a membrane protein. The supporting entity is attached to the receptor mol. at an end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferably gated. Such membranes may be used in the formation of sensing devices. A lipid gramicidin surface was prepd. on a Pd-coated glass electrode. The 1st monolayer contd. dodecanethiol:gramicidin (30:1) and the 2nd monolayer contd. 1-O-[11-(p-vinylphenoxy)undecanoyl]-2-O-octadecyl-3-O-acetoylglycerol (prepn. given): gramicidin R (prepd. by reacting gramicidin, 11-chloro-3,6,9-trioxaundec-1-yl succinate, dicyclohexyldiimide, and diethylaminopyridine) (100:1). The electrode was then incubated in an Fab soln. contg. Fab from 2 monoclonal antibodies to 2 distinct sites on human chorionic gonadotropin (hCG). HCG at 0.96 ng/mL in 0.1M NaCl gave an impedance of 106.20 .OMEGA. at 10 mHz corresponding to 4.8 .times. 104 conducting gramicidin channels, measured at 1 mHz. Before hCG, the impedance was 106.15 .OMEGA. at 10 mHz arising from 5.9 .times. 104 conducting gramicidin channels at 1 mHz.

L215 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:109177 CAPLUS
DOCUMENT NUMBER: 108:109177
TITLE: Single channel recordings of reconstituted ion channel proteins: an improved technique
AUTHOR(S): Keller, Bernhard U.; Hedrich, Rainer; Vaz, Winchil L.; Criado, Manuel
CORPORATE SOURCE: Abt. Membranbiophys. Mol. Biol., Max-Planck-Inst. Biophys. Chem., Goettingen, D-3400, Fed. Rep. Ger.
SOURCE: Pfluegers Arch. (1988), 411(1), 94-100
CODEN: PFLABK; ISSN: 0031-6768
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Single channel recording of reconstituted ion channels is possible by patch clamp measurements of giant liposomes formed by dehydration-rehydration of lipid films. This hydration technique consists of carefully controlled dehydration of a suspension of small vesicles followed by rehydration of the residue resulting in formation of large liposomes. Patch pipets can be attached to the liposome surface, yielding stable, **high resistance** seals between membranes and glass pipets. This method allows the study of the properties of reconstituted ion channels from different tissues. The hydration technique was used to characterize the reconstituted K+-channel of sarcoplasmic reticulum from rabbit skeletal muscle. In a soln. of 100 mM KCl, the sarcoplasmic reticulum K+ channel studied displays a conductance .gamma.K+ of 145 pS. The single channel conductance in 100 mM Rb+ and Na+ is .gamma.Rb+ = 98 pS and .gamma.Na+ = 65 pS resp. A concn. of 0.5 mM decamethonium causes a flickering channel block. These properties are in good agreement with the ones found in sarcoplasmic reticulum K+-channels characterized by other methods. Other ion channels have also been reconstituted and studied by this technique. This improved method is

compared with previous approaches and its applicability for the characterization of reconstituted ion channel proteins is discussed.

L215 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:100427 CAPLUS
DOCUMENT NUMBER: 96:100427
TITLE: Method for studying **ionic channels** in excitable membranes
AUTHOR(S): Bedukidze, Z. A.; Zil'berter, Yu. I.; Timin, E. N.
CORPORATE SOURCE: Moscow, USSR
SOURCE: Avtometriya (1981), (4), 22-8
CODEN: AVMEBI
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Methods for studying ionic channels in excitable membranes are discussed in relation to channel populations (1-100, 102-104, and 104-106), methods for resolving the current signals, and devices for registering the signals. Math. equations are extensively discussed for 2- and 3-electrode systems.

L215 ANSWER 33 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:548046 BIOSIS
DOCUMENT NUMBER: PREV200100548046
TITLE: Whole-cell recordings from new planar patch clamp **electrodes.**
AUTHOR(S): Osipchuk, Y. (1); Dromaretcky, A. (1); Savtchenko, A. (1); Yang, I. (1); Mathes, C. (1); Churchward, P. (1); Kleinschmidt, J. (1); Smith-Maxwell, C. (1); Blatz, A. (1)
CORPORATE SOURCE: (1) Axon Instruments, Inc., Union City, CA USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1583. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The next major advancement in patch clamp recording techniques lays in the development of planar patch clamp arrays allowing parallel recordings for **high throughput screening** (HTS). Novel planar patch voltage clamp **electrodes** were made from polydimethylsiloxilane (PDMS), commonly known as Sylgard. **Electrode** hole diameters measured approximately 1-3 mum. Fabrication of the **electrodes** affords high band-width, low noise recordings. Recordings were made with N1E-115 neuroblastoma cells, derived from mouse sympathetic ganglion cells. Standard internal and external saline solutions were used for patch clamp recordings. Various whole-cell current types were recorded (i.e., Na, K, and Ca currents). These new planar patch clamp **electrodes** represent the next step toward parallel recording in many chambers simultaneously. Parallel patch clamp recordings enables direct, mass **screening** of **ion-channel** drugs for the first time. Our results indicate that primary **screening** with direct, high information content measurements of ionic currents is now feasible.

L215 ANSWER 34 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:312419 BIOSIS
DOCUMENT NUMBER: PREV200100312419
TITLE: High-resistance MDCK-C7 monolayers used for measuring invasive potency of tumour cells.
AUTHOR(S): Zak, Jan; Schneider, Stefan Werner; Eue, Ines; Ludwig, Thomas; Oberleithner, Hans (1)

CORPORATE SOURCE: (1) Department of Physiology, University of Muenster, Robert-Koch-Str. 27a, D-48149, Muenster: oberlei@uni-muenster.de Germany
SOURCE: Pfluegers Archiv European Journal of Physiology, (May, 2000) Vol. 440, No. 1, pp. 179-183. print. ISSN: 0031-6768.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We describe an electrophysiological method for evaluating the intrinsic invasive potency of tumour cells using renal cells as an in vitro assay system. A high-resistance clone of Madin-Darby canine kidney cells (MDCK-C7) was grown to confluency in a filter cup. Transepithelial **electrical resistance** across the MDCK-C7 monolayer was measured in a commercially available **electrode** chamber. After a transepithelial **electrical resistance** of about 4,000 OMEGA cm2 had been reached, human melanoma or pancreatic carcinoma cells were co-cultivated with the MDCK-C7 monolayer. Both carcinoma cell lines induced resistance breakdown measured after 24 h or later depending on seeding density and cell type. Seeding carcinoma cells on the basolateral surface of MDCK-C7 cells caused a similar decrease in **transepithelial resistance** of the MDCK-C7 monolayer. Resistance breakdown indicates opening of tight junctions prior to tumour cell invasion. In conclusion, the high-resistance MDCK-C7 cell clone could serve as a valuable biological assay system to determine electrically the metastatic potency of tumour cells in vitro.

L215 ANSWER 35 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:114999 BIOSIS
DOCUMENT NUMBER: PREV200100114999
TITLE: **Ion channel** functional analysis using electrical stimulation.
AUTHOR(S): Maher, M. P. (1); Gonzalez, J. E.
CORPORATE SOURCE: (1) Aurora Biosciences Corporation, San Diego, CA USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-713.6. print. Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We present a **high throughput** method for electrical stimulation and optical recording of rapid signals from voltage-gated **ion channels**. To this end we have built a **high -throughput** 96-well plate reader to assay cultured cell lines engineered to express stably a target **ion channel**. We use **electrodes** to create homogenous electric fields across microtiter wells. **Membrane** potential changes that result from charge movement through the channel is continuously monitored using FRET-based voltage probes whose sensitivity isapprx 1% fluorescence ratio change per millivolt. This method is effective for rapid **screening** of unknown compounds against therapeutically relevant **ion channel** targets, including voltage-gated sodium, **potassium** , and **chloride channels**. To illustrate the utility of this approach we **screened** a portion of our compound library to characterize novel blockers of voltage-gated **sodium channel** in the absence of chemical modifiers. Agonists and antagonists of this channel can be detected, as they alter the response relative to control conditions. The method is particularly useful for functional characterization of pharmacologically active compounds. By measuring the **membrane** properties with and without a drug under

various stimulation conditions, it might be possible to describe the biophysical properties of drug action.

L215 ANSWER 36 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:90953 BIOSIS
DOCUMENT NUMBER: PREV199900090953
TITLE: Local transport regions (LTRs) in human stratum corneum due to long and short 'high voltage' pulses.
AUTHOR(S): Pliquett, Uwe F. (1); Vanbever, Rita; Preat, Veronique; Weaver, James C.
CORPORATE SOURCE: (1) Fac. Chem., PCIII, Univ. Bielefeld, D-33615 Bielefeld Germany
SOURCE: Bioelectrochemistry and Bioenergetics, (Nov., 1998) Vol. 47, No. 1, pp. 151-161.
ISSN: 0302-4598.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Application of 'high voltage' (HV) pulses (transdermal voltage Uskin > 50 V) to preparations of human skin have been previously hypothesized to cause electroporation of multilamellar lipid barriers within the stratum corneum (SC). Such pulses cause large increases in molecular transport and decrease in the skin's **electrical resistance**. Here we describe the local transport regions (LTRs) and the surrounding local dissipiation regions (LDRs) that dominate the skin's response to both 'long' and 'short' HV pulses. The number of LTR/LDRs depends on Uskin, but their size depends on pulse duration, so that LDRs can merge to form large regions containing several LTRs. LTRs themselves are not spatially homogeneous, as they have a ringlike structure, which is interpreted as involving different transport behavior viz. aqueous pathways which are either predominantly perpendicular or parallel to the SC. Our observations are consistent with the hypothesis that localized aqueous pathway formation (electroporation) occurs first, followed by secondary processes involving the entry of water into the SC and also localized heating.

L215 ANSWER 37 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:481638 BIOSIS
DOCUMENT NUMBER: PREV199699196894
TITLE: Applications of impedance spectroscopy in biochemistry and biophysics.
AUTHOR(S): Janshoff, Andreas; Wegener, Joachim; Steinem, Claudia; Sieber, Manfred; Galla, Hans-Joachim
CORPORATE SOURCE: Inst. fuer Biochemie, Westfaelische Wilehelms-Univ. Muenster, Wilhelm-Klemm-Str. 2, 48149 Muenster Germany
SOURCE: Acta Biochimica Polonica, (1996) Vol. 43, No. 2, pp. 339-348.
ISSN: 0001-527X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The present study is intended to demonstrate the application of impedance spectroscopy to two very different fields of biophysical research. The core component of our measuring setup is a self-constructed continuous wave impedance spectrometer together with special measuring chambers which are individually designed for the systems under investigation. We directed our attention towards: i) the investigation of solid supported lipid bilayers in general, especially systems which are suitable for protein reconstitution such as dimethyldioctadecylammonium bromide (DODAB) immobilized onto a gold **electrode**, precovered with a negatively charged monolayer of 3-mercaptopropionic acid. Impedance spectroscopy allows to study the stability, the thickness and the **electrode** coverage of those artificial **membranes** as well as the observation of **ion transport** mediated by **ionophores** like gramicidin D incorporated into a DODAB-bilayer. ii) The characterization of the passive electrical properties of

epithelial and endothelial cell monolayers in general and especially the determination of their transepithelial (transendothelial) **electrical resistances** as a measure for epithelial barrier function. From impedance spectra, as reported here, we are able to follow the formation and modulation of cell layer permeability to small ions.

L215 ANSWER 38 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:499841 BIOSIS
DOCUMENT NUMBER: PREV199598523391
TITLE: Effects of decreasing **electrical resistance** in Characeae cell **membranes** caused by the flow of alternating current.
AUTHOR(S): Spiewla, Edward; Tokarska-Schlattner, Malgorzata
CORPORATE SOURCE: Dep. Physics, Tech. Univ. Lublin, Bernardynska 13, 20-950 Lublin Poland
SOURCE: Acta Societatis Botanicorum Poloniae, (1995) Vol. 63, No. 3-4, pp. 269-273.
ISSN: 0001-6977.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English; Polish
AB By means of the techniques of external **electrodes** and microelectrodes, it was found that evanescent flow of an alternating current through plasmalemma of Characeae cells neutralises oscillatory change in their **electrical resistance** and reversibly diminishes its value. This effect is particularly significant in the case of "high resistance cells", but it weakens with increasing temperature. The value of the estimated activation energy indicates that, after flow of the alternating current through the **membrane**, a rapid increase in the conductivity may be caused by an increase in conductivity of **potassium channels**. This result seems to support the hypothesis of electroconformational feedback.

L215 ANSWER 39 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:342089 BIOSIS
DOCUMENT NUMBER: PREV199497355089
TITLE: Voltage clamping of xenopus laevis oocytes utilizing agarose-cushion **electrodes**.
AUTHOR(S): Schreibmayer, Wolfgang (1); Lester, Henry A.; Dascal, Nathan
CORPORATE SOURCE: (1) Div. Biol., California Inst. Technol., Pasadena, CA 91125 USA
SOURCE: Pfluegers Archiv European Journal of Physiology, (1994) Vol. 426, No. 5, pp. 453-458.
ISSN: 0031-6768.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Two-**electrode** voltage clamping of expressed **ion channels** in intact oocytes of the South African clawed frog Xenopus laevis has been refined to allow stable, low-**resistance** **electrical** access to the cytosol (50-800 k-OMEGA). Glass microelectrodes were filled with a cushion of 1% agarose at their tips to prevent KCl leakage (agarose-cushion **electrodes**). Insertion of these **electrodes** into X. laevis oocytes yielded stable preparations for periods of more than 1 h with a stable input resistance of 1-4 M-OMEGA. Furthermore, a simple modification of the voltage-clamp circuit (charging compensator) is described that increases the flexibility of arrangements for differential recording of the **membrane** potential in order to subtract voltage drops across a series resistance. The result is a considerable increase in the practically attainable speed of the voltage clamp with the conventional two-**electrode** arrangement. The performance of the charging compensator was tested on an

equivalent circuit that simulates the oocyte and **electrodes**. In addition, the combination of agarose-cushion **electrodes** and the charging compensator was tested on oocytes expressing Shaker H4 currents. The fidelity of the voltage-clamp circuit was also verified by measuring the **membrane** potential with additional independent microelectrodes connected to a differential amplifier, independent of the two-**electrode** voltage clamp system. The system described here will be useful for **ion channel** studies in X. laevis oocytes requiring long-term recordings and/or measurements of large, fast ion currents.

L215 ANSWER 40 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1986:264766 BIOSIS
DOCUMENT NUMBER: BA82:19515
TITLE: CELL MEMBRANES AND PARACELLULAR RESISTANCES IN ISOLATED RENAL PROXIMAL TUBULES FROM RABBIT AND AMBYSTOMA.
AUTHOR(S): BELLO-REUSS E
CORPORATE SOURCE: DEPARTMENT OF CELL BIOLOGY AND PHYSIOLOGY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, SAINT LOUIS, MO. 63110, USA.
SOURCE: J PHYSIOL (LOND), (1986) 370 (0), 25-38.
CODEN: JPHYA7. ISSN: 0022-3751.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Transepithelial specific resistance (Re) was measured in isolated and perfused rabbit proximal convoluted tubules by cable analysis and intracellular micro-**electrode** techniques were used to calculate the **electrical resistances** of the cell membranes and of the paracellular pathway. Re was 16 .+-. 2 .OMEGA. cm2 and the space constant was 130 .+-. 14 .mu.m, n = 29. Re was significantly increased by a decrease in temperature from 37 to 10.degree. C, and was practically abolished by nominal removal of Ca2+ from the bathing solution (to 2.0 .+-. 0.3 .OMEGA. cm2, P < 0.001, n = 6). The apparent ratio of cell membrane resistances (luminal to basolateral) was 3.1 .+-. 0.3. The control values of apical and basolateral membrane resistances (Ra and Rb) were calculated from the values of (1) Re, (2) the apparent ratio of cell membrane resistances, and (3) the effects of addition of either Ba2+ (1 mM) to the bath solution or glucose (8 mM) to the perfusate on basolateral and apical membrane voltages (assuming that the initial effects of Ba2+ and glucose are restricted to the ipsilateral membrane). Control values of Ra (.OMEGA. cm2 of epithelium) were 249 .+-. 68 (Ba2+ method) and 227 .+-. 42 (glucose method). Values of Rb were 70 .+-. 11; and 66 .+-. 12, respectively. The low paracellular resistance values obtained with the Ba2+ and glucose methods, respectively, 17 .+-. 5 and 15 .+-. 1 .OMEGA. cm2, explain the low **transepithelial resistance**. The use of the Ba2+ and glucose methods provides alternatives to cell cable determinations for the calculation of cell membrane resistances. Cell membrane and shunt resistances measured by the same methods in isolated perfused Ambystoma tigrinum proximal tubules (in .OMEGA. cm2 of epithelium) were: Ra, 2650 .+-. 180 (glucose method) and 2368 .+-. 350 (Ba2+ method). Values of Rb were 665 .+-. 99 (glucose method) and 701 .+-. 124 (Ba2+ method). The paracellular resistance values were 58 .+-. 11 (glucose method) and 84 .+-. 12 (Ba2+ method). These results are in good agreement with previously reported values obtained by intracellular cable analysis (Maunsbach & Boulpaep, 1984).

L215 ANSWER 41 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1984:283462 BIOSIS
DOCUMENT NUMBER: BA78:19942
TITLE: ACTIVE **POTASSIUM ION TRANSPORT** ACROSS THE CATERPILLAR SPODOPTERA-LITTORALIS MID GUT 2. INTRA CELLULAR MICRO **ELECTRODE** STUDIES.
AUTHOR(S): THOMAS M V; MAY T E
CORPORATE SOURCE: SHELL RES. LIMITED, SITTINGBOURNE RES. CENT.,

SITTINGHBOURNE, ME9 8AG, UK.
SOURCE: J EXP BIOL, (1984) 108 (0), 293-304.
CODEN: JEBIAM. ISSN: 0022-0949.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Intracellular microelectrodes were used to record from individual cells in midguts isolated from S. littoralis caterpillars. Recorded potentials, referenced to the basal (hemolymph) surface, showed a bimodal distribution, with maxima in the ranges 0 to -10 and -30 to -40 mV. In experiments where the fluorescent dye Lucifer Yellow CH was ionophoresed from the recording microelectrode, fluorescence was associated with single cells only for **membrane** potentials more negative than -25 mV. Examination of tissue sections showed these cells to be of both columnar and goblet types, in an approximate 2:1 ratio. This conclusion conflicts with that of a previous study on other caterpillar species, in which it was concluded that the goblet cells had basal **membrane** potentials of only a few mV. Attempts to discriminate between the 2 cell types by resistance measurements were unsuccessful. The resistance values obtained were substantially higher than those in the previous study, although they are consistent with those predicted from the overall tissue **resistance**. The major **electrical** effect of K+ transport inhibition by 1 m-KCN was on the apical **membrane**, supporting the view that the K+ pumps is located there. The major initial effect of K+ removal was on the basal **membrane**, which is as expected if this **membrane** is permeable primarily to K+. The inability to discriminate between goblet and columnar cells by any electrical criterion suggests that both cell types may be able to transport K+.

L215 ANSWER 42 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1983:290349 BIOSIS
DOCUMENT NUMBER: BA76:47841
TITLE: MICRO **ELECTRODE** STUDIES OF NECTURUS-MACULOSUS ANTRAL MUCOSA **ELECTRICAL** POTENTIALS AND **RESISTANCES**.
AUTHOR(S): GRADY T P; CHEUNG L Y
CORPORATE SOURCE: DEP. OF SURGERY, WASHINGTON UNIV. SCH. OF MED., ST. LOUIS, MO. 63110.
SOURCE: AM J PHYSIOL, (1983) 244 (1), G71-G75.
CODEN: AJPHAP. ISSN: 0002-9513.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Intracellular microelectrode techniques were applied to N. maculosus antral mucosa. Stable intracellular impalements were obtained with 15-50 M.OMEGA. microelectrodes filled with 3M KCl. It was possible to change rapidly the mucosal bathing solution while maintaining the microelectrode in the cell. With these techniques, the **electrical** potentials and **resistances** of the cell membranes and the shunt pathway were measured. The transepithelial potential was -4.9 .+-. 13 mV, serosal solution reference. Apical cell membrane potential was -43.9 .+-. 0.6 mV, cell negative to the mucosal solution. Basolateral cell membrane potential was -48.8 .+-. 1.3 mV, cell negative to serosal solution. **Transepithelial resistance** was 427 .+-. 66 .OMEGA. .cntdot. cm2. The ratio of apical to basolateral membrane resistances was 3.4 .+-. 0.3. The **electrical resistances** of the transcellular and paracellular pathway were determined by the measurement of the total **transepithelial resistance** and the ratio of apical to basolateral cell membrane resistances before and after blocking apical membrane Na permeability with amiloride. The resistances of the apical cell membrane, basolateral cell membrane and the shunt were 2203 .+-. 585, 1296 .+-. 384 and 604 .+-. 81 .OMEGA. .cntdot. cm2, respectively (mean .+-. SE). Calculations from these measurements indicate that the shunt contribution to transepithelial conductance was .apprx. 85%.

L215 ANSWER 43 OF 61 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1977:143986 BIOSIS
DOCUMENT NUMBER: BA63:38850
TITLE: AN IN-VIVO METHOD FOR CONTINUOUS REGISTRATION OF ELECTROLYTE CONCENTRATIONS IN THE BLOOD OF AQUATIC ANIMALS.
AUTHOR(S): SPAARGAREN D H
SOURCE: NETH J SEA RES, (1976) 10 (2), 215-222.
CODEN: NJSRBA. ISSN: 0077-7579.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable
AB The **electrical resistance** measured between 2 disparate-sized **electrodes** placed 1 in each of 2 compartments containing electrolyte solutions and separated by a semi-permable **membrane** were related to the specific resistances, and hence to ionic concentrations, of the solutions in the 2 compartments. Different sensitivities for the concentrations in the 2 compartments could be achieved by altering the relative sizes of the 2 **electrodes**, the highest sensitivity being obtained in the compartment with the relatively smaller-surfaced **electrode**. This principle for measuring blood electrolyte concentration was tested in Carcinus maenas. A 4-**electrode** system eliminated **electrode** resistance. Gill resistance for **ion transport** was very low compared to the resistance of medium and blood.

L215 ANSWER 44 OF 61 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1992:22354109 BIOTECHNO
TITLE: Polymer membranes in clinical sensor applications II. The design and fabrication of permselective hydrogels for electrochemical devices
AUTHOR: Murphy S.M.; Hamilton C.J.; Davies M.L.; Tighe B.J.
CORPORATE SOURCE: Speciality Materials Research Group, Aston University, Aston Triangle, Birmingham B4 7ET, United Kingdom.
SOURCE: Biomaterials, (1992), 13/14 (979-990)
CODEN: BIMADU ISSN: 0142-9612
DOCUMENT TYPE: Journal; General Review
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

L215 ANSWER 45 OF 61 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1982:12100002 BIOTECHNO
TITLE: Amiloride: A molecular probe of **sodium transport** in tissues and cells
AUTHOR: Benos D.J.
CORPORATE SOURCE: Dept. Physiol. Biophys., Harvard Med. Sch., Boston, MA 02115, United States.
SOURCE: American Journal of Physiology - Cell Physiology, (1982), 11/2 (C131-C145)
CODEN: AJPCDD
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AB The potassium-sparing diuretic amiloride has proven to be a useful pharmacological tool for elucidating the molecular basis and physiological regulation of facilitated sodium entry in tissue and cells. There are two general classes of Na.sup.+ transport mechanisms which are sensitive to this drug: 1) a conductive Na.sup.+ entry pathway found in **electrically high resistance** epithelia and 2) a Na.sup.+-H.sup.+ electroneutral exchange system found in certain leaky epithelia such as the renal proximal tubule. This latter system is also found in many different cellular preparations and seems to function in cell proliferation and differentiation, volume regulation, and

intracellular pH regulation. In these cells, this exchange pathway becomes operational usually after some external stimuli. Much higher concentrations of amiloride are required to inhibit the exchange pathway than those required to inhibit the Na.sup.+ entry pathway. This drug is the most potent and specific inhibitor of Na.sup.+ entry found to date and thus affords the opportunity to be used as a label for the isolation of these transport moieties.

L215 ANSWER 46 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001378092 EMBASE
TITLE: Channel activity of a phytotoxin of Clavibacter michiganense ssp. nebraskense in tethered **membranes**
AUTHOR: Michalke A.; Galla H.-J.; Steinem C.
CORPORATE SOURCE: C. Steinem, Institut fur Biochemie, Westfalische Wilhelms-Universitat, Wilhelm-Klemm-Strasse 2, 48149 Munster, Germany. steinec@uni-muenster.de
SOURCE: European Biophysics Journal, (2001) 30/6 (421-429).
Refs: 43
ISSN: 0175-7571 CODEN: EBJOE8
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
027 Biophysics, Bioengineering and Medical Instrumentation
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Solid-supported **membranes** immobilized on gold electrodes were used to detect and characterize the spontaneously inserting anion-selective protein channel (Clavibacter anion channel, CAC) present in the culture fluid of Clavibacter michiganense ssp. nebraskense. Three different **membrane** systems varying in the composition of the first chemisorbed monolayer were investigated by means of impedance spectroscopy. Conductance changes of the immobilized lipid **membranes** were sensitively detected after adding the culture fluid of the bacteria to the solid-supported **membranes**, indicating that the relative change in conductance is largest if the lipid layer is attached to the surface via a flexible lipid anchor. Variation in the d.c. potential revealed that CAC exhibits a voltage dependence in these tethered **membranes** which can be described by an exponential function in accordance with previous results obtained from patchclamp measurements and impedance analysis. The addition of an inhibitor that selectively blocks anion channels abolished the channel conductance almost completely, indicating that the increased conductivity can be attributed to the specific insertion of the CAC. A linear dependence of the channel conductance on the chloride concentration was found, which was modulated by the charges of the second lipid monolayer. The results demonstrate that tethered lipid **membranes** on gold surfaces in conjunction with impedance spectroscopy allows one to monitor and characterize water-soluble spontaneously inserting channels, providing an effective means to probe for bacterial toxins.

L215 ANSWER 47 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001197414 EMBASE
TITLE: Rapid inhibition of the Na(+)-K(+) pump affects Na(+)-Ca(2+) exchanger-mediated relaxation in rabbit ventricular myocytes.
AUTHOR: Terracciano C.M.N.
CORPORATE SOURCE: C.M.N. Terracciano, Imperial College School of Medicine, National Heart and Lung Institute, Cardiac Medicine, Dovehouse Street, London SW3 6LY, United Kingdom. c.terracciano@ic.ac.uk

SOURCE: Journal of Physiology, (15 Mar 2001) 533/1 (165-173).
Refs: 29
ISSN: 0022-3751 CODEN: JPHYA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB 1. The direct influence of Na(+)-K(+) pump activity on the ability of the Na(+)-Ca(2+) exchanger to remove Ca(2+) was investigated in isolated adult rabbit ventricular myocytes. 2. Cell shortening was measured using an edge-detection system. Cytoplasmic [Ca(2+)] was monitored using the fluorescent indicator indo-1. Electrophysiological parameters were recorded using **high-resistance** microelectrodes. The Na(+)-K(+) pump was rapidly inhibited by removal of extracellular K(+) and measurements were taken almost immediately to minimise effects on other cellular compartments. Activity of the Na(+)-Ca(2+) exchanger was monitored during release of Ca(2+) from the sarcoplasmic reticulum (SR) elicited by rapid application of 15 mM caffeine. 3. When Na(+)-K(+) pump activity was affected by K(+) removal, cell relaxation and indo-1 fluorescence decline were slowed by approximately 40%. The charge calculated by integrating the caffeine-induced transient inward current was unchanged, suggesting that there was no difference in the SR Ca(2+) content in the two conditions. However Ca(2+) flux via the Na(+)-Ca(2+) exchanger was slower when the Na(+)-K(+) pump was inhibited. 4. Similar experiments were performed by inhibiting the Na(+)-K(+) pump using 0.5 mM strophanthidin. In this condition similar results to the ones observed by K(+) removal were obtained, suggesting a specific role of the Na(+)-K(+) pump in the phenomenon observed. 5. This study suggests that the activity of the Na(+)-K(+) pump influences Na(+)-Ca(2+) exchanger function in the absence of changes in SR Ca(2+) content. This can be explained by a slower removal of Na(+) from the subsarcolemmal space. The source of the increase in subsarcolemmal [Na(+)] requires further investigation. However, calculations derived from modelling suggest that the Na(+)-Ca(2+) exchanger itself could be involved.

L215 ANSWER 48 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000040471 EMBASE
TITLE: Trans/paracellular, surface/crypt, and epithelial/subepithelial resistances of mammalian colonic epithelia.
AUTHOR: Gitter A.H.; Bendfeldt K.; Schulzke J.D.; Fromm M.
CORPORATE SOURCE: A.H. Gitter, Institut fur Klinische Physiologie, Universitatsklin. Benjamin Franklin, Freie Universitat Berlin, D-12200 Berlin, Germany. gitter@medizin.fu-berlin.de
SOURCE: Pflugers Archiv European Journal of Physiology, (2000) 439/4 (477-482).
Refs: 27
ISSN: 0031-6768 CODEN: PFLABK
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The epithelial barrier function of the large intestine resides in the trans- and paracellular pathways of the surface epithelium and crypts. Conventional transmural resistance and permeability measurements, however, yield only the resistance of the whole tissue and not that of its individual components. Combining conductance scanning techniques and impedance analysis, we determined the resistance of epithelial and subepithelial tissues, crypts and surface epithelium, and trans- and paracellular pathways of the mouse distal colon. The subepithelial tissue

contributed 15% to the transmural resistance of 118 .+-. 9 .OMEGA..cntdot.cm2. In the epithelium proper the resistance of crypts (429 .+-. 86 .OMEGA..cntdot.cm2) exceeded that of the surface epithelium (132 .+-. 15 .OMEGA..cntdot.cm2). The paracellular resistance (3.2 .+-. 0.4 k.OMEGA..cntdot.cm2) of the surface epithelium was 23-fold higher than the transcellular resistance (137 .+-. 16 .OMEGA..cntdot.cm2), and thus the epithelium was classified as 'medium tight'. In order to investigate the trans- and paracellular resistances of the crypt epithelium as well, flat monolayers of HT-29/B6 cultured colon crypt cells were studied, which had a **transepithelial resistance** of 349 .+-. 32 .OMEGA..cntdot.cm2. With transcellular resistance (377 .+-. 41 .OMEGA..cntdot.cm2) tenfold lower than the paracellular resistance (3.9 .+-. 1.3 k.OMEGA..cntdot.cm2), this cryptal monolayer was also classified as 'medium tight'. Hence, considering the 1.2 times larger area of the crypt epithelium, the surface epithelium has a 4 times larger ion permeability than the crypt epithelium. However, the paracellular resistances are not different. Thus the lower transcellular resistance of the surface compared to the crypt epithelium suggests a higher density of ion channels in the apical **membrane** of surface cells.

L215 ANSWER 49 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97194737 EMBASE
DOCUMENT NUMBER: 1997194737
TITLE: Impedance analysis of ion transport through gramicidin channels incorporated in solid supported lipid bilayers.
AUTHOR: Steinem C.; Janshoff A.; Galla H.-J.; Sieber M.
CORPORATE SOURCE: C. Steinem, Institute of Biochemistry, Westfalische Wilhelms-University, Wilhelm-Klemm-Strasse 2, D-48149 Munster, Germany
SOURCE: Bioelectrochemistry and Bioenergetics, (1997) 42/2 (213-220).
Refs: 20
ISSN: 0302-4598 CODEN: BEBEBP
PUBLISHER IDENT.: S 0302-4598(96)05113-6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The topic of this study is a solid supported lipid bilayer consisting of dimethyldioctadecylammoniumbromide (DODAB) and the channel-forming polypeptide, gramicidin D, from Bacillus brevis immobilized on gold electrodes. The peptide was reconstituted into large unilamellar vesicles of DODAB which were fused on a negatively charged monolayer of 3-mercaptopropionic acid. The peptide forms a pore of 4 .ANG. diameter, selective for monovalent cations. The sequence of conductivity of monovalent alkaline cations is Cs+ > K+ > Na+ > Li+. The transport of these monovalent cations through this supported lipid bilayer via the gramicidin dimer was observed by a.c. impedance spectroscopy as an integral electrochemical method. Only a single bilayer preparation was necessary to perform the whole measurement. The obtained data were analysed with an equivalent circuit based on the theory developed by de Levie. We succeeded in confirming the sequence of the conductivity by impedance spectroscopy. The conductance of the **membrane** shows a linear dependence on the concentration of the cations in the bulk phase. This system is therefore recommended for biosensor devices based on ion transport through solid supported **membranes**.

L215 ANSWER 50 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95090409 EMBASE
DOCUMENT NUMBER: 1995090409
TITLE: Single-microelectrode voltage clamp measurements of pancreatic .beta.-cell **membrane** ionic currents in

situ.
AUTHOR: Rojas E.; Stokes C.L.; Mears D.; Atwater I.
CORPORATE SOURCE: Laboratory of Cell Biology, Mathematical Research Branch, National Institutes of Health, NIDDK,Bethesda, MD 20893, United States
SOURCE: Journal of Membrane Biology, (1995) 143/1 (65-77). ISSN: 0022-2631 CODEN: JMBBBO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A conventional patch clamp amplifier was used to test the feasibility of measuring whole-cell ionic currents under voltage clamp conditions from .beta.-cells in intact mouse islets of Langerhans perifused with bicarbonate Krebs buffer at 37.degree.C. Cells impaled with a **high resistance** microelectrode (ca. 0.150 G.OMEGA.) were identified as .beta.-cells by the characteristic burst pattern of electrical activity induced by 11 mM glucose. Voltage-dependent outward K+ currents were enhanced by glucose both in the presence and absence of physiological bicarbonate buffer and also by bicarbonate regardless of the presence or absence of glucose. For comparison with the usual patch clamp protocol, similar measurements were made from single rat .beta.-cells at room temperature; glucose did not enhance the outward currents in these cells. Voltage-dependent inward currents were recorded in the presence of tetraethylammonium (TEA), an effective blocker of the K+ channels known to be present in the .beta.-cell **membrane**. Inward currents exhibited a fast component with activation-inactivation kinetics and a delayed component with a rather slow inactivation; inward currents were dependent on Ca2+ in the extracellular solution. These results suggest the presence of either two types of voltage-gated Ca2+ channels or a single type with fast and slow inactivation. We conclude that it is feasible to use a single intracellular microelectrode to measure voltage-gated **membrane** currents in the .beta.-cell within the intact islet at 37.degree.C, under conditions that support normal glucose-induced insulin secretion and that glucose enhances an as yet unidentified voltage-dependent outward K+ current.

L215 ANSWER 51 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94256503 EMBASE
DOCUMENT NUMBER: 1994256503
TITLE: Effect of ouabain on **membrane** conductances and volume in A6 cells.
AUTHOR: Granitzer M.; Mountian I.; De Smet P.; Van Driessche W.
CORPORATE SOURCE: Laboratory for Physiology, Katholieke Universiteit Leuven, Campus Gasthuisberg,B-3000 Leuven, Belgium
SOURCE: Renal Physiology and Biochemistry, (1994) 17/5 (223-231). ISSN: 1011-6524 CODEN: RPBIEL
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
028 Urology and Nephrology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The present study reports the effect of a reduction in the Na+-transport rate on cell volume. A decrease in transport rate was achieved by inhibition of the basolateral Na+/K+ pump with ouabain. Cultured A6 cell monolayers were short-circuited and exposed to ouabain at the basolateral surface. In one series of experiments, cells were impaled with microelectrodes to measure cell voltage, apical fractional resistance and

thus derive **membrane** conductances. Another set, A6, served for cell height measurements. Ouabain decreased short-circuit current (I(sc)), which is an index of transepithelial Na+ transport: the reduction in transport rate varied from 26 to 79% within 10 min. Equivalent circuit analysis revealed a 20% decrease in apical **membrane** conductance (g(a)), whereas basolateral **membrane** conductance (g(b)) increased by 66%. A decrease in cell voltage (12 mV) together with drop in g(a) during ouabain may account for the reduction in I(sc). The rise in g(b) is mainly due to a gain in Cl- conductance which increased from 114 to 613 .mu.S/cm2, compatible with activation of Cl- channels. All of this occurs without a detectable change in cell height. We may conclude from these data that inhibition of Na+ exit by ouabain is quickly compensated by a decrease in apical Na+ entry and an increase in basolateral Cl- conductance. Constant cell volume during ouabain implies that the total cell solute is essentially unchanged.

L215 ANSWER 52 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93191163 EMBASE
DOCUMENT NUMBER: 1993191163
TITLE: Harmonic system analysis of the algae Valonia utricularis: Contribution of an electrogenic transport system to gain and phase-shift of the transfer function.
AUTHOR: Wang J.; Wehner G.; Benz R.; Zimmermann U.
CORPORATE SOURCE: Lehrstuhl fur Biotechnologie, Biozentrum der Universitat Wurzburg,D-8700 Wurzburg, Germany
SOURCE: Biophysical Journal, (1993) 64/6 (1657-1667).
ISSN: 0006-3495 CODEN: BIOJAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cell **membrane** properties of the giant marine alga Valonia utricularis were measured in the frequency domain between 1 Hz and 10 MHz by harmonic system analysis. Harmonic analysis was performed by imposing a sinusoidal electrical voltage on the cell interior via an internal microelectrode. Gain and phase- shift of the resulting sinusoidal **membrane** voltage were measured over the whole frequency range with an internal voltage microelectrode. Bode plots of gain and phase-shift allowed the determination of the electrical parameters of the equivalent electronic circuits of the cell **membrane** of V. utricularis, which showed dynamic and passive properties dependent on the pH of the external aqueous solution. The dynamic components of the **membrane** impedance were caused by an electrogenic transport system for chloride described previously (Wang, J., G. Wehner, R. Benz, and U. Zimmermann. 1991. Biophys. J. 59:235-248). The kinetic and equilibrium parameters of the transport system could be evaluated from the fit of Bode plots of gain and phase- shift. The frequency domain technique revealed complete agreement of transport parameters with previously published results. The data demonstrate that an electrogenic transport system can be driven by an oscillating electric field.

L215 ANSWER 53 OF 61 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92364849 EMBASE
DOCUMENT NUMBER: 1992364849
TITLE: Sodium- and chloride-conductive pathways in cultured mouse tracheal epithelium.
AUTHOR: Clarke L.L.; Burns K.A.; Bayle J.-Y.; Boucher R.C.; Van Scott M.R.
CORPORATE SOURCE: Pulmonary Div., Dept. of Medicine, University of North Carolina,Chapel Hill, NC 27599-7020, United States

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (1992) 263/5 7-5 (L519-L525). ISSN: 0002-9513 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The utility of a transgenic murine model of cystic fibrosis (CF) lung disease will likely depend on whether the mouse's proximal airway epithelium is characterized by Na+- and Cl--conductive pathways comparable to those found in human airways. Therefore, the electrophysiological properties of primary cultures of mouse tracheal epithelium (MTE) were investigated using double-barreled, Cl--selective microelectrodes. Epithelial cells isolated from freshly excised mouse tracheae formed confluent polarized monolayers on permeable collagen supports and developed significant transepithelial potential differences (.apprx.-10 mV) within 5-6 days postseeding. Under basal conditions, the MTE monolayers had an equivalent short-circuit current (I(eq)) of -21.1 .+-. 2.1 .mu.A/cm2 and a **transepithelial resistance** of 424 .+-. 49 .OMEGA. .cntdot. cm2. Intracellular measurements indicated that the apical (V(a)) and basolateral (V(b)) **membrane** potential differences were -16.9 .+-. 1.5 and - 25.4 .+-. 1.5 mV, respectively; apical **membrane** fractional resistance was 0.36 .+-. 0.03; and intracellular Cl- activity was 56.1 .+-. 2.3 mM. The presence of an apical Na+ conductance was demonstrated by luminal amiloride application (10-4 M), which decreased I(eq), hyperpolarized V(a), and increased the fractional resistance of the apical **membrane**. The presence of an apical Cl- conductance was demonstrated by substitution of Cl- with gluconate in the luminal bath, which decreased intracellular Cl- activity and increased the fractional resistance of the apical **membrane**. Regulation of the Cl- conductance was tested by exposing MTE to isoproterenol (10-4 M, luminal), which increased I(eq) by activating a depolarizing conductance in the apical **membrane**. Luminal application of ATP (10-4 M) was also found to increase the rate of Cl- secretion. We conclude that ion transport in MTE, like normal human airway epithelia, is characterized by 1) a significant amiloride-sensitive Na+ conductance in the apical **membrane** and 2) an apical **membrane** Cl--conductive pathway that can be regulated by .beta.-adrenergic agonists.

L215 ANSWER 54 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-195894 [25] WPIDS
DOC. NO. NON-CPI: N2002-148792
DOC. NO. CPI: C2002-060590
TITLE: Biological activity determination of candidate compound for drug discovery, involves repetitively exposing compound-exposed-cells to electric field, monitoring transmembrane potential changes, without patch clamp.
DERWENT CLASS: B04 **S03**
INVENTOR(S): GONZALEZ, J E; MAHER, M P
PATENT ASSIGNEE(S): (GONZ-I) GONZALEZ J E; (MAHE-I) MAHER M P; (AURO-N) AURORA BIOSCIENCES CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002008748	A2	20020131	(200225)*	EN	146

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002025568 A1 20020228 (200225)
US 2002025573 A1 20020228 (200225)
US 2002028480 A1 20020307 (200225)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002008748 A2		WO 2001-US21652	20010709
US 2002025568 A1	Provisional	US 2000-217671P	20000710
		US 2001-804480	20010312
US 2002025573 A1	Provisional	US 2000-217671P	20000710
		US 2001-804458	20010312
US 2002028480 A1	Provisional	US 2000-217671P	20000710
		US 2001-804580	20010312

PRIORITY APPLN. INFO: US 2001-804580 20010312; US 2000-217219P 20000710; US 2000-217221P 20000710; US 2000-217666P 20000710; US 2000-217671P 20000710; US 2001-804457 20010312; US 2001-804458 20010312; US 2001-804480 20010312

AB WO 200208748 A UPAB: 20020418
NOVELTY - Determination of biological activity of a candidate compound involves exposing one or more cells to the compound, repetitively exposing the cells to one or more electric fields so as to effect a controlled charge in transmembrane potential of the cells, and monitoring changes in the transmembrane potential of the cells, without using a patch clamp.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) Assaying the biochemical activity of the compound against a target **ion channel**;

(b) Assaying **ion channel** activity; and

(c) Modifying transmembrane potential of cell

USE - For use in drug discovery, analysis, screening test compounds against **ion-channels** in these organelles, profiling, and for determining state-dependent pharmacological activity of compounds against **ion channel** and **transporter** proteins.

ADVANTAGE - The transmembrane potentials of intact living cells comprising at least one voltage regulated **ion channel**, can be precisely modulated via the application of repetitive electrical stimulation pulses through the fluid bathing the cells. The method provides accurate and reliable modulation of the transmembrane potentials of intact living cells without significantly disrupting their native cellular integrity. The method is reliable and specific in regulating the **membrane** potential of living cells that are compatible with optic methods of analysis and are readily amendable to **high throughput** analysis.

DESCRIPTION OF DRAWING(S) - The figure shows a dipper **electrode** array.
Dwg.1a/31

L215 ANSWER 55 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-281740 [29] WPIDS
DOC. NO. NON-CPI: N2001-200892
DOC. NO. CPI: C2001-085674
TITLE: Plane substrate for patch clamp apparatus useful in determining and/or monitoring e.g. current through cell **membranes**, includes first surface part having

sites providing high **electrical resistance** seal.

DERWENT CLASS: B04 **S03**
INVENTOR(S): BECH, M; CHRISTOPHERSEN, P; DUE, J; HANSEN, O; OLESEN, S P; PETERSEN, J W; TELLEMAN, P; THOMSEN, L
PATENT ASSIGNEE(S): (SOPH-N) SOPHION BIOSCIENCE AS
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001025769	A2	20010412	(200129)*	EN	31

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000074065 A 20010510 (200143)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001025769	A2	WO 2000-DK548	20001002
AU 2000074065	A	AU 2000-74065	20001002

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000074065	A	Based on	WO 200125769

PRIORITY APPLN. INFO: DK 1999-1407 19991001

AB WO 200125769 A UPAB: 20010528
NOVELTY - A plane substrate having a first surface part and a second opposite surface part useful in determining and/or monitoring e.g. current through cell **membranes** is new.

DETAILED DESCRIPTION - The plane substrate (12) has two surface parts, and carries reference **electrodes**. The first surface part has sites, each holding an **ion channel**-containing structure and measuring **electrode**. The reference and measuring **electrodes** generate a current between them when they are in electrolytic contact with each other and when potential difference is applied between them. Each site provides a high **electrical resistance** seal between **ion channel**-containing structures. The seal separates a domain on one side of the structure in electrolytic contact with the measuring **electrode** from a domain on the other side of the structure in electrolytic contact with reference **electrode**, so that a current flowing through the **ion channels** between the **electrodes** can be determined and/or monitored. The **electrodes** are integrated with the substrate and formed by wafer processing technology.

An INDEPENDENT CLAIM is also included for a method for establishing a whole cell measuring configuration for determining and/or monitoring an electrophysiological property of **ion channels** of one or more comprising:

(1) providing a substrate as defined above;

(2) supplying a carrier liquid at one or more sites, the carrier liquid containing one or more **ion channel**-containing structures;

(3) positioning at least one of the **ion channel**-containing structures at a corresponding number checking for a high

electrical resistance seal between an **ion channel**-containing structure held at a site and the surface part of the site with which the high **electrical resistance** seal is to provided by successively applying a first electric potential difference between the measuring **electrode** associated with the site and a reference **electrode**, monitoring a first current flowing between the measuring **electrode** and the reference **electrode**, and comparing the first current to a predetermined threshold current and, if the first current is at most the predetermined threshold current, then approving the site as having an acceptable seal between the **ion channel**-containing structure and the surface part of the site; and

(4) establishing a whole-cell configuration at approved sites, where a third current flowing through **ion channels** of the **ion channel**-containing structure between the measuring **electrode** and the reference **electrodes** can be determined and/or monitored.

USE - For patch clamp apparatus useful in determining and/or monitoring electrophysiological properties, e.g. current through **ion channels** or voltage clamp, or capacitance, through **ion channel**-containing structures e.g., cell **membranes**.

ADVANTAGE - The inventive substrate has **high throughput** and reliability. It allows effective and fast measurement of cells.

DESCRIPTION OF DRAWING(S) - The drawing shows a cross sectional side view of the inventive substrate.

Plane substrate 12
Measuring **electrode** 16
Silica surface part 22
Layer of hydrophobic material 26
Silver chloride 28

Dwg.3A/7

L215 ANSWER 56 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-371110 [31] WPIDS
DOC. NO. NON-CPI: N1999-276693
DOC. NO. CPI: C1999-109576
TITLE: In vitro simulation of biological dissolution of pharmaceutical formulation and absorption of pharmaceutically active compound.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): ANDERSON, K E; TAM, Y K
PATENT ASSIGNEE(S): (ANDE-I) ANDERSON K E; (TAMY-I) TAM Y K
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9928437	A1	19990610	(199931)*	EN	38
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9913284	A	19990616	(199945)		
US 6022733	A	20000208	(200014)		
EP 1034251	A1	20000913	(200046)	EN	
R: AT BE CH DE DK ES FI FR GB IT LI NL SE					
CN 1284127	A	20010214	(200130)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9928437	A1	WO 1998-CA1090	19981130
AU 9913284	A	AU 1999-13284	19981130
US 6022733	A	US 1997-982692	19971202
EP 1034251	A1	EP 1998-956732	19981130
		WO 1998-CA1090	19981130
CN 1284127	A	CN 1998-813408	19981130

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9913284	A	Based on	WO 9928437
EP 1034251	A1	Based on	WO 9928437

PRIORITY APPLN. INFO: US 1997-982692 19971202

AB WO 9928437 A UPAB: 19990806

NOVELTY - Biological dissolution of a pharmaceutical formulation is simulated by first determining its dissolution profile in an apical medium. Then its rate of absorption by a cell monolayer is determined when opposite surfaces of the monolayer are exposed to the medium and a basal medium respectively.

DETAILED DESCRIPTION - A system for assessment of simulated biological dissolution of a pharmaceutical formulation (F) and absorption of a pharmaceutically active compound (B) comprises:

(1) a dissolution chamber for determining the dissolution profile of (F) in a medium at the apical surface of a cell monolayer;

(2) a cell culture chamber for absorption of (B) by the cell monolayer comprising:

(a) a housing;

(b) a tubular filter permeable to medium and supporting the cell monolayer on its surface, and forming apical and basal chambers in the housing;

(3) means for supply and outflow of basal medium to the basal chamber, and apical medium to the apical chamber.

The medium flowing from the dissolution chamber containing (F) is introduced to the apical chamber , and the rate of appearance of (B) in the medium outflowing from the basal chamber is analyzed to determine absorption of (B).

USE - Determining the in vitro-in vivo correlation of a pharmaceutical composition or dosage form (claimed).

Dwg.1/3

L215 ANSWER 57 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1998-610520 [51] WPIDS
DOC. NO. NON-CPI: N1999-052004
DOC. NO. CPI: C1999-021223
TITLE: Patch clamp study of **ion** transfer **channels** in biological **membranes** - by automatic positioning of patch pipette over microperfusion chamber by digitizing image of cells and pipette tip into pixels.
DERWENT CLASS: B04 D16 J04 **S03**
INVENTOR(S): BECH, M; CHRISTOPHERSEN, P; OLESEN, S
PATENT ASSIGNEE(S): (NEUR-N) NEUROSEARCH AS
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9850791	A1	19981112	(199851)*	EN	82

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW
AU 9872054 A 19981127 (199915)
EP 980523 A1 20000223 (200015) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 729397 B 20010201 (200112)
NZ 337814 A 20010427 (200128)
JP 2002507278 W 20020305 (200220) 82

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9850791	A1	WO 1998-DK167	19980429
AU 9872054	A	AU 1998-72054	19980429
EP 980523	A1	EP 1998-919082	19980429
		WO 1998-DK167	19980429
AU 729397	B	AU 1998-72054	19980429
NZ 337814	A	NZ 1998-337814	19980429
		WO 1998-DK167	19980429
JP 2002507278	W	JP 1998-547642	19980429
		WO 1998-DK167	19980429

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9872054	A	Based on	WO 9850791
EP 980523	A1	Based on	WO 9850791
AU 729397	B	Previous Publ.	AU 9872054
		Based on	WO 9850791
NZ 337814	A	Based on	WO 9850791
JP 2002507278	W	Based on	WO 9850791

PRIORITY APPLN. INFO: DK 1997-1151 19971008; DK 1997-496 19970501; DK 1997-902 19970801

AB WO 9850791 A UPAB: 19990217
Automatic **electrode** positioning apparatus for connecting **electrode** to a cell, comprising chamber for cells; adjacent movable **electrode**; **electrode** positioning means; means for measuring an electrical parameter, electrically connected to **electrode** and chamber and forming electrical circuit; and controller for controlling positioning means in response to parameter determinations so that **electrode** can be automatically connected to a selected cell. A method is also claimed.
USE - Studying electrical events in cell **membranes**, such as studying **ion** transfer **channels** in biological **membranes** by patch clamp techniques.
ADVANTAGE - The apparatus allows novel electrophysiology drug handling and screening for chemical substances or compounds. **High throughput** is achieved using low volume solutions and samples.
Dwg.0/26

L215 ANSWER 58 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-371431 [37] WPIDS
DOC. NO. NON-CPI: N1996-312422
DOC. NO. CPI: C1996-117929
TITLE: Ligands for integral **membrane** protein DEC - useful in compsns. to target molecules to partic. areas

of the body, e.g. for immune modulation, and to induce immune suppression.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): JIANG, W; NUSSENZWEIG, M C; STEINMAN, R M; SWIGGARD, W J
PATENT ASSIGNEE(S): (UYRQ) UNIV ROCKEFELLER
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9623882	A1	19960808	(199637)*	EN	152
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP MX US					
AU 9649702	A	19960821	(199648)		
EP 808366	A1	19971126	(199801)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
JP 10513350	W	19981222	(199910)		173
MX 9705923	A1	19980701	(200012)		
AU 716056	B	20000217	(200019)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9623882	A1	WO 1996-US1383	19960131
AU 9649702	A	AU 1996-49702	19960131
EP 808366	A1	EP 1996-906258	19960131
		WO 1996-US1383	19960131
JP 10513350	W	JP 1996-523726	19960131
		WO 1996-US1383	19960131
MX 9705923	A1	MX 1997-5923	19970731
AU 716056	B	AU 1996-49702	19960131

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9649702	A	Based on	WO 9623882
EP 808366	A1	Based on	WO 9623882
JP 10513350	W	Based on	WO 9623882
AU 716056	B	Previous Publ.	AU 9649702
		Based on	WO 9623882

PRIORITY APPLN. INFO: US 1995-381528 19950131
AB WO 9623882 A UPAB: 19960918
A novel method for identifying a ligand for DEC which is an integral **membrane** protein expressed by dendritic cells, thymic, lung and small intestine epithelial cells, and brain capillaries, which has an apparent mol.wt. of 205 kD (PAGE) and which comprises 10 lectin domains, a transmembrane domain and a short cytoplasmic tail contg. a coated pit localisation consensus sequence, comprises: (a) contacting a protein comprising >1 DEC lectin domain with a ligand; and (b) detecting ligand binding with the DEC lectin domain; where detection of binding of the candidate ligand and the DEC indicates that the candidate ligand is a ligand for DEC.

USE - The ligand is used in compsns. (claimed) to specifically target molecules, partic. antibiotics or anti-cancer, anti-viral, anti-parasitic or anti-inflammatory drugs, to areas of the body, e.g. the pulmonary or intestinal circulation, pulmonary airways, lumen of the small intestine, dendritic cells in the skin, and T cell areas of lymphoid organs, thymus or brain. This can be useful e.g. for immune modulation, **trans-epithelial** transport, and crossing the blood-brain barrier. The ligand can also be used in a compsn. (claimed) to induce immune

suppression in which an allergen or autoantigen (partic. myelin basic protein, collagen or a fragment, DNA, a nuclear protein, a nucleolar protein, mitochondrial protein or pancreatic beta-cell protein) is conjugated to the ligand, where the compsn. lacks immune stimulatory agents. The vector can introduce genes into cells for gene therapy. Dwg.0/25

L215 ANSWER 59 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-239593 [24] WPIDS
DOC. NO. NON-CPI: N1996-200489
DOC. NO. CPI: C1996-076544
TITLE: Appts. for measuring effect of cpds. on **ion** -transfer **channels** of **membrane** - comprises auto-sampler, container for supporting liq., perfusion chamber, patch pipette and **electrodes** esp. for rapid, large scale drug screening.
DERWENT CLASS: B04 D16 **S03**
INVENTOR(S): CHRISTOPHERSEN, P; OLESEN, S
PATENT ASSIGNEE(S): (NEUR-N) NEUROSEARCH AS
COUNTRY COUNT: 65
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9613721	A1	19960509	(199624)*	EN	48
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG					
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KG KP KR KZ LK LR LT LV MD MG MN MX NO NZ PL RO RU SG SI SK TJ TM TT UA US UZ VN					
AU 9527886	A	19960523	(199635)		
EP 788600	A1	19970813	(199737)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
JP 10509794	W	19980922	(199848)		45
US 6063260	A	20000516	(200031)		
US 6117291	A	20000912	(200046)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9613721	A1		WO 1995-EP2204	19950607
AU 9527886	A		AU 1995-27886	19950607
EP 788600	A1		EP 1995-923258	19950607
			WO 1995-EP2204	19950607
JP 10509794	W		WO 1995-EP2204	19950607
			JP 1996-514270	19950607
US 6063260	A		WO 1995-EP2204	19950607
			US 1997-836094	19970425
US 6117291	A	Div ex	WO 1995-EP2204	19950607
		Div ex	US 1997-836094	19970425
			US 1999-237085	19990125

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9527886	A	Based on	WO 9613721
EP 788600	A1	Based on	WO 9613721
JP 10509794	W	Based on	WO 9613721
US 6063260	A	Based on	WO 9613721

PRIORITY APPLN. INFO: DK 1994-1252 19941028
AB WO 9613721 A UPAB: 20001006
Appts. for determining the effect of a cpd. (A) on **ion**-transfer

channels in a **membrane** comprises: (1) an autosampler which automatically withdraws test samples from containers and discharges them into a receptacle; (2) a container for supporting liq. (SL); (3) a perfusion chamber (PC) that receives sample, SL and the **membrane**, including a reference **electrode** in contact with soln.; (4) systems for supplying liq. to, and removing it from, PC, (5) a patch pipette, including an **electrode**, that can be moved over the PC to produce a seal of high **electrical resistance** with the surface of a patch of **membrane** in the PC; (6) electrical connections between pipette and reference **electrodes** for measuring the current flowing between them, before and after adding test sample.

Also new is a micro-perfusion chamber assembly consisting of a base (with aperture) and a transparent cover over the bottom of the base to define a chamber. It also includes a reference **electrode**, systems for adding/removing liq. and an electrical connection for the **electrode** to a measuring circuit.

USE - The method is used to screen (A) for electro-physiological activity. It is partic. useful for rapid large scale drug screening.

ADVANTAGE - The appts. provides **high throughput** and the micro-PC requires only very small amts. of sample and SL, so that tests can be completed quickly.

Dwg.2/12

L215 ANSWER 60 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1992-097537 [13] WPIDS
DOC. NO. NON-CPI: N1992-072960
TITLE: Vertical transport chamber for electro-physiological epithelia study - provides exchangeable test surfaces with measurement openings as small as 0.5 mm in adjustable halves.
DERWENT CLASS: P81 R16 **S03**
INVENTOR(S): SCHWARZ, H J; SCHWARZ, H
PATENT ASSIGNEE(S): (SCHW-I) SCHWARZ H
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4020013	A	19920319	(199213)*		5
DE 4020013	C2	20000316	(200018)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4020013	A	DE 1990-4020013	19900621
DE 4020013	C2	DE 1990-4020013	19900621

PRIORITY APPLN. INFO: DE 1990-4020013 19900621
AB DE 4020013 A UPAB: 19931006
The device consists of two flat half chambers and is suitable for adjustment under a stereo or binocular microscope while the sample is being introduced. Micro-samples in physiological or other media are placed in drops direct onto the inner sides of the half chambers. The epithelia are studied under constant conditions, and erfusion of the epitheila may be at equal or asymmetric pressures on on either side. Half-maximal mass transfer of the substances in the perfusion solution is provided ina few seconds, using substances such as inhibitors of **ion transport** and pH regulation; hormones; pharmaceutical/poison mixt.; substrates such as sugar, amino-acids, fats, fatty acids; and eco-toxicoiogical contaminates such as cadmium, lead etc.

Reversibility, irreversibility and other kinetic parameters represented by electrophysicological quantities such as the **trans -epithelial** potential difference, short-circuit current, resistance etc. are measured.

USE/ADVANTAGE - Study of **transport** of **ions** etc. in tissues (epithelia, cuticles) of organs and organisms. Pharmacology, eco-toxicology and transport-physiology. Allows study of smaller samples having a min. measuring surface dia. of about 0.5 mm.

1/1

L215 ANSWER 61 OF 61 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1987-242261 [34] WPIDS
DOC. NO. NON-CPI: N1987-181305
DOC. NO. CPI: C1987-102374
TITLE: Appts. studying cell migration across monolayer of epithelial cells - while measuring **trans-epithelial electrical resistance.**
DERWENT CLASS: A89 D16 S01 **S03**
INVENTOR(S): CONYERS, G P; CRAMER, E B; MILKS, L C; PEREZ, A; VALENTI, A
PATENT ASSIGNEE(S): (UYNY-N) STATE UNIV NEW YORK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4686190	A	19870811	(198734)*		11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4686190	A	US 1986-831147	19860219

PRIORITY APPLN. INFO: US 1986-831147 19860219

AB US 4686190 A UPAB: 19930922

An appts. is used to study cell migration and for the measurement of **electrical resistance** across a monolayer of the cells.

The appts. includes internal and external chambers with a substrate across one end of the internal chamber on which are growing a confluent layer of cells. The internal chamber is positioned within the external one so that the layer of cells is contacted by a first fluid on one surface and a second fluid on its other surface. A pair of bridges consisting of a current passing bridge and a voltage recording bridge are positioned on either side of the substrate.

The appts. comprises a cylinder (J) forming the internal chamber and an external chamber (A) formed at its lower end as a well with a fluid outlet (G). The lower, open-end of the cylinder (J) is closed by a substrate (L) on which the cells are grown. Voltage and current bridges (F,F',H,H') are positioned either side of the substrate. A stainless steel punch (not shown) may be used to remove uniform discs from the substrate without damaging or separating the epithelial monolayer from its substrate. The internal and external cylinders may be formed of cellulose acetate or nitrate, of polycarbonate or of connective tissue.

USE - The device is used for the in vitro study of cell migration across a monolayer of epithelial cells while measuring the transepithelia **electrical resistance** of the monolayer. It may be used to study granuloma formation in tuberculosis of sarcoidosis and the effects of drug therapy, or to study migration of cancer cells from one organ to another.

5/11

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